```
     (FILE 'HOME' ENTERED AT 15:45:30 ON 29 SEP 2003)

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     15:45:38 ON 29 SEP 2003
                E SCHUBERT
                E E3 AND WALTER
                E SCHUBERT
L1            1 S E3 AND WALTER
L2            1 S E3 AND WALTER
L3          229 S E3 AND CELL
L4            5 S L3 AND TARGET

     FILE 'STNGUIDE' ENTERED AT 15:52:18 ON 29 SEP 2003
L5            0 S CELL SPECIFIC TARGET AND PROCESS
L6            0 S CELL SPECIFIC TARGET
L7            0 S CELL- SPECIFIC TARGET
L8            0 S CELL- SPECIFIC AND SCHUBERT
L9            0 S MELK
L10           4 S PROTEOMICS

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     16:06:49 ON 29 SEP 2003

     FILE 'STNGUIDE' ENTERED AT 16:07:16 ON 29 SEP 2003

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     16:07:32 ON 29 SEP 2003
L11       16796 S PROTEOMIC?
L12           1 S L11 AND MELK
L13        2438 S PROTEOMIC AND PROCESS
L14           8 S L13 AND CULTIVATED
L15        1282 S L13 AND CELL
L16           0 S L15 AND SCHUBERT
L17          15 S L15 AND HETEROGENEOUS
L18           1 S L15 AND PROTEIN CHIPS
L19           4 S L15 AND AUTOMATIC?

     FILE 'STNGUIDE' ENTERED AT 16:21:29 ON 29 SEP 2003

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     16:25:49 ON 29 SEP 2003
L20          27 S L15 AND ENDOTHELI?
L21          16 DUP REM L20 (11 DUPLICATES REMOVED)

=>
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FILE 'HOME' ENTERED AT 15:45:30 ON 29 SEP 2003

=> FIL BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'SCISEARCH' ENTERED AT 15:45:38 ON 29 SEP 2003
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=> e schubert
E1           69     SCHUBERGI/BI
E2            1     SCHUBERL/BI
E3         1378 --> SCHUBERT/BI
E4            1     SCHUBERTA/BI
E5           33     SCHUBERTELLA/BI
E6            2     SCHUBERTELLID/BI
E7            4     SCHUBERTELLIDAE/BI
E8            2     SCHUBERTELLINAE/BI
E9            2     SCHUBERTELLINIDS/BI
E10          22     SCHUBERTH/BI
E11          33     SCHUBERTI/BI
E12           1     SCHUBERTIA/BI

=> e e3 and walter
E1            1     E2ZZ/BI
E2        26428     E3/BI
E3            0 --> E3 AND WALTER/BI
E4            2     E3.0/BI
E5            1     E3.10/BI
E6            1     E3.10.4K/BI
E7            1     E3.2.1.21/BI
E8            5     E3.3/BI
E9            1     E3.39.214/BI
E10           2     E3.4/BI
E11           1     E3.49/BI
E12          48     E3.5/BI

=> e schubert
E1           69     SCHUBERGI/BI
E2            1     SCHUBERL/BI
E3         1378 --> SCHUBERT/BI
E4            1     SCHUBERTA/BI
E5           33     SCHUBERTELLA/BI
E6            2     SCHUBERTELLID/BI
E7            4     SCHUBERTELLIDAE/BI
```

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E8            2      SCHUBERTELLINAE/BI
E9            2      SCHUBERTELLINIDS/BI
E10          22      SCHUBERTH/BI
E11          33      SCHUBERTI/BI
E12           1      SCHUBERTIA/BI

=> s e3 and walter
L1            1 SCHUBERT/BI AND WALTER

=> d l1 ibib abs

L1   ANSWER 1 OF 1     MEDLINE on STN
ACCESSION NUMBER:    84269013     MEDLINE
DOCUMENT NUMBER:     84269013   PubMed ID: 6748618
TITLE:               Psychometric principles in the selection, interpretation,
                     and evaluation of communication self-assessment
                     inventories.
AUTHOR:              Demorest M E; Walden B E
SOURCE:              JOURNAL OF SPEECH AND HEARING DISORDERS, (1984 Aug) 49 (3)
                     226-40.
                     Journal code: 0376335. ISSN: 0022-4677.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         198409
ENTRY DATE:          Entered STN: 19900320
                     Last Updated on STN: 19900320
                     Entered Medline: 19840905
AB   A variety of self-assessment inventories have been introduced in recent
     years for use with hearing-impaired patients.  These instruments differ
     considerably, both conceptually and operationally.  Audiologists,
     therefore, are faced with the task of selecting a test instrument that is
     appropriate to their patient population and testing purpose.  This paper
     outlines the psychometric principles that guide the selection,
     interpretation, and evaluation of self-assessment inventories.  The
     application of these principles to a specific clinical population is
     illustrated by three studies of the Hearing Performance Inventory (Giolas,
     Owens, Lamb, & Schubert, 1979) conducted at Walter
     Reed Army Medical Center (WRAMC).


=> s e3 and walter
L2            1 SCHUBERT/BI AND WALTER

=> s e3 and cell
L3          229 SCHUBERT/BI AND CELL

=> s l3 and target
L4            5 L3 AND TARGET

=> d l4 1-5 ibib abs

L4   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         1999:432073  CAPLUS
DOCUMENT NUMBER:          131:75469
TITLE:                    Convection in the presence of a first-order phase
                          change
AUTHOR(S):                Sakurai, Shinichi; Tschammer, Armin; Pesch, Werner;
                          Ahlers, Guenter
CORPORATE SOURCE:         Department of Physics and Center for Nonlinear
                          Science, University of California at Santa Barbara,
```

Santa Barbara, CA, 93106, USA
SOURCE: Physical Review E: Statistical Physics, Plasmas, Fluids, and Related Interdisciplinary Topics (1999), 60(1), 539-550
CODEN: PLEEE8; ISSN: 1063-651X
PUBLISHER: American Physical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We report exptl. and theor. results for two-phase convection in a thin horizontal layer of a fluid with a first-order phase change and heated from below. A top layer of the nematic phase of a liq. crystal is located above the bottom layer of the isotropic phase of the same substance. A horizontal field of 1000 G is applied to align the director of the nematic phase. Over some ranges of the thickness of the isotropic phase, and in sufficiently large thermal gradients, the more dense nematic phase can be stably stratified above the less dense isotropic one, with a stable interface between them. Based on the equations of motion derived for this problem by Busse and **Schubert** [J. Fluid Mech. 46, 801 (1971)], we evaluate the bifurcation lines between the quiescent and convecting states and the corresponding crit. wave vectors as a function of the interface position. We report exptl. measurements based on Nusselt-no. detns. for the locations of the bifurcation lines. They are in good agreement with the theor. results. We also report approx. detns. of the crit. wave nos. which are semiquant. consistent with the theory. A great diversity of patterns is obsd. in the convecting states, including normal and parallel rolls, rolls with defects and disorder, **target** patterns and spirals, and cellular flow with upflow or downflow at the **cell** center. These patterns are discussed in terms of the breaking of the mirror symmetry at the horizontal midplane by the interface, and in terms of the orienting effects of the magnetic field.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1977:565312 CAPLUS
DOCUMENT NUMBER: 87:165312
TITLE: Selective **cell** adhesion of neuronal **cell** lines
AUTHOR(S): Santala, Roger; Gottlieb, David I.; Littman, Daniel; Glaser, Luis
CORPORATE SOURCE: Dep. Biol. Chem., Washington Univ., St. Louis, MO, USA
SOURCE: Journal of Biological Chemistry (1977), 252(21), 7625-34
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cloned neural **cell** lines derived from ethylnitrosourea-treated rat embryos (**Schubert**, D., et al, 1974) adhered preferentially to monolayers of **cells** obtained by dissocn. of neural tissue of either chick or rat embryos. One such cloned line, B103, will bind to **cells** obtained from any of the major regions of the embryonal nervous system, but bound only poorly to other types of **cells**. A plasma membrane-enriched fraction prepd. from B103 **cells** showed the same relative binding characteristics to embryonal neural and nonneural **cells** as intact B103 **cells**. Treatment of the membranes with trypsin at low concns. or treatment of the **target cells** with low concns. of glutaraldehyde or HCHO also abolished binding. A very similar binding pattern to that of B103 **cells** and plasma membranes was shown by B50 and B65 **cells** and plasma membranes in that both of these **cell** lines bound preferentially to monolayers prepd. from **cells** from embryonal nervous tissue. The plasma membranes from these **cells** however

showed significant differences in binding to other cultured neural **cell** lines. Apparently, only a part of the **cells** adhesive components is retained on the isolated plasma membrane, and there may be several adhesive components on each **cell** type. The cloned neural **cells** are apparently a suitable model system for the study of selective **cell** adhesion.

L4 ANSWER 3 OF 5 MEDLINE on STN
ACCESSION NUMBER: 2002244253 MEDLINE
DOCUMENT NUMBER: 21966828 PubMed ID: 11969793
TITLE: Convection in the presence of a first-order phase change.
AUTHOR: Sakurai S; Tschammer A; Pesch W; Ahlers G
CORPORATE SOURCE: Department of Physics and Center for Nonlinear Science, University of California at Santa Barbara, Santa Barbara, California 93106, USA.
SOURCE: PHYSICAL REVIEW. E, STATISTICAL PHYSICS, PLASMAS, FLUIDS, AND RELATED INTERDISCIPLINARY TOPICS, (1999 Jul) 60 (1) 539-50.
Journal code: 9887340. ISSN: 1063-651X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020502
Last Updated on STN: 20020829
Entered Medline: 20020827

AB We report experimental and theoretical results for two-phase convection in a thin horizontal layer of a fluid with a first-order phase change and heated from below. A top layer of the nematic phase of a liquid crystal is located above the bottom layer of the isotropic phase of the same substance. A horizontal field of 1000 G is applied in order to align the director of the nematic phase. Over some ranges of the thickness of the isotropic phase, and in sufficiently large thermal gradients, the more dense nematic phase can be stably stratified above the less dense isotropic one, with a stable interface between them. Based on the equations of motion derived for this problem by Busse and **Schubert** [J. Fluid Mech. 46, 801 (1971)], we evaluate the bifurcation lines between the quiescent and convecting states and the corresponding critical wave vectors as a function of the interface position. We report experimental measurements based on Nusselt-number determinations for the locations of the bifurcation lines. They are in good agreement with the theoretical results. We also report approximate determinations of the critical wave numbers which are semiquantitatively consistent with the theory. A great diversity of patterns is observed in the convecting states, including normal and parallel rolls, rolls with defects and disorder, **target** patterns and spirals, and cellular flow with upflow or downflow at the **cell** center. These patterns are discussed in terms of the breaking of the mirror symmetry at the horizontal midplane by the interface, and in terms of the orienting effects of the magnetic field.

L4 ANSWER 4 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 78229198 EMBASE
DOCUMENT NUMBER: 1978229198
TITLE: Selective **cell** adhesion of neuronal **cell** lines.
AUTHOR: Santala R.; Gottlieb D.I.; Littman D.; Glaser L.
CORPORATE SOURCE: Div. Biol. Biomed. Sci., Dept. Biol. Chem., Washington Univ., St Louis, Mo. 63110, United States
SOURCE: Journal of Biological Chemistry, (1977) 252/21 (7625-7634).
CODEN: JBCHA3

COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English

AB Cloned neural **cell** lines derived from ethylnitrosourea-treated rat embryos (**Schubert**, D., Heinemann, S., Carlisle, W., Tarikas, H., Kimes, B., Patrick, J., Steinbach, J. H., Culp, W., and Brandt, B. L. (1974) Nature 249, 224-227) adhere preferentially to monolayers of **cells** obtained by dissociation of neural tissue of either chick or rat embryos. One such cloned line, B103, has been investigated in some detail. B103 **cells** will bind to **cells** obtained from any of the major regions of the embryonal nervous system. B103 **cells** will bind only poorly to chick embryo fibroblasts, Chinese hamster ovary **cells**, or embryonal liver **cells** from either the chick or the rat. A plasma membrane-enriched fraction prepared from B103 **cells** shows the same relative binding characteristics to embryonal neural and non-neural **cells** as intact B103 **cells**. Treatment of the membranes with trypsin at low concentrations or treatment of the **target cells** with low concentrations of glutaraldehyde or formaldehyde also abolishes binding. Binding does not take place at 0.degree.. A very similar binding pattern to that of B103 **cells** and plasma membranes is shown by B50 and B65 **cells** and plasma membranes in that both of these **cell** lines bind preferentially to monolayers prepared from **cells** from embryonal nervous tissue. The plasma membranes from these **cells** however show significant differences in binding to other cultured neural **cell** lines. It is suggested that only a part of the **cells** adhesive components is retained on the isolated plasma membrane and that there may be several adhesive components on each **cell** type. The cloned neural **cells** appear to be a suitable model system for the study of selective **cell** adhesion.

L4 ANSWER 5 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:589964 SCISEARCH
THE GENUINE ARTICLE: 218KC
TITLE: Convection in the presence of a first-order phase change
AUTHOR: Sakurai S (Reprint); Tschammer A; Pesch W; Ahlers G
CORPORATE SOURCE: UNIV CALIF SANTA BARBARA, DEPT PHYS, SANTA BARBARA, CA 93106 (Reprint); UNIV CALIF SANTA BARBARA, CTR NONLINEAR SCI, SANTA BARBARA, CA 93106; KYOTO INST TECHNOL, DEPT POLYMER SCI & ENGN, SAKYO KU, KYOTO 6068585, JAPAN; UNIV BAYREUTH, INST PHYS, D-95440 BAYREUTH, GERMANY
COUNTRY OF AUTHOR: USA; JAPAN; GERMANY
SOURCE: PHYSICAL REVIEW E, (JUL 1999) Vol. 60, No. 1, pp. 539-550. Publisher: AMERICAN PHYSICAL SOC, ONE PHYSICS ELLIPSE, COLLEGE PK, MD 20740-3844.
ISSN: 1063-651X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We report experimental and theoretical results for two-phase convection in a thin horizontal layer of a fluid with a first-order phase change and heated from below. A top layer of the nematic phase of a liquid crystal is located above the bottom layer of the isotropic phase of the same. substance. A horizontal field of 1000 G is applied in order to align the director of the nematic phase. Over some ranges of the thickness of the isotropic phase, and in sufficiently large thermal gradients, the more dense nematic phase can be stably stratified above the less dense

isotropic one, with a stable interface between them. Based on the equations of motion derived for this problem by Busse and **Schubert** [J. Fluid Mech. 46, 801 (1971)], we evaluate the bifurcation lines between the quiescent and convecting states and the corresponding critical wave vectors as a function of the interface position. We report experimental measurements based on Nusselt-number determinations for the locations of the bifurcation lines. They are in good agreement with the theoretical results. We also report approximate determinations of the critical wave numbers which are semiquantitatively consistent with the theory. A great diversity of patterns is observed in the convecting states, including normal and parallel rolls, rolls with defects and disorder, **target** patterns and spirals, and cellular flow with upflow or downflow at the **cell** center. These patterns are discussed in terms of the breaking of the mirror symmetry at the horizontal midplane by the interface, and in terms of the orienting effects of the magnetic field. [S1063-651X(99)05707-4].

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=> FIL STNGUIDE
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    34.99      35.20

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 26, 2003 (20030926/UP).

=> s cell specific target and process
            16 CELL
            29 SPECIFIC
            20 TARGET
             0 CELL SPECIFIC TARGET
                 (CELL(W)SPECIFIC(W)TARGET)
            14 PROCESS
            14 PROCESSES
            23 PROCESS
                 (PROCESS OR PROCESSES)
L5           0 CELL SPECIFIC TARGET AND PROCESS

=> s cell specific target
            16 CELL
            29 SPECIFIC
            20 TARGET
L6           0 CELL SPECIFIC TARGET
                 (CELL(W)SPECIFIC(W)TARGET)

=> s cell- specific target
            16 CELL
            29 SPECIFIC
            20 TARGET
L7           0 CELL- SPECIFIC TARGET
                 (CELL(W)SPECIFIC(W)TARGET)

=> s cell- specific and schubert
```

```
            16 CELL
            29 SPECIFIC
             0 CELL- SPECIFIC
                 (CELL(W)SPECIFIC)
             0 SCHUBERT
L8           0 CELL- SPECIFIC AND SCHUBERT

=>  s MELK
             0 MELK
L9           0 MELK

=> s proteomics
L10          4 PROTEOMICS

=> d l1o 1-4 ibib abs
'L1O' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'
'IBIB' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'
'ABS' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'

The following are valid formats:

The default display format is GEN.

GEN --- AN, DBN, DESC, PROD
DBS --- AN, DBN, DESC, SUBJ, SI, DATA, UA, PROD,
        SUPP, REPR, SFIELD, PROP, DFIELD, TFIELD,
        FEAT, EXAMPLE
ALL --- AN, DBN, DESC, SUBJ, CC, SI, DATA, UA, NTE,
        PROD, SUPP, REPR, SFIELD, PROP, DFIELD, TFIELD,
        FEAT, PRICE, EXAMPLE
COVERAGE - AN, DBN, SUBJ, CC, SI, DATA
FIELDS --- AN, DBN, SFIELD, PROP, DFIELD, TFIELD
HIT ------ All fields containing hit terms
KWIC ----- All fields containing hit terms
OCC ------ List of display fields containing hit terms

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'GEN';
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The same formats (except for HIT, KWIC, and OCC) may be used
with the DISPLAY ACC command to display the record for a
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ENTER DISPLAY FORMAT (GEN):s proteomicsend
'S' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'
'PROTEOMICSEND' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'

The following are valid formats:

The default display format is GEN.

GEN --- AN, DBN, DESC, PROD
DBS --- AN, DBN, DESC, SUBJ, SI, DATA, UA, PROD,
        SUPP, REPR, SFIELD, PROP, DFIELD, TFIELD,
        FEAT, EXAMPLE
ALL --- AN, DBN, DESC, SUBJ, CC, SI, DATA, UA, NTE,
```

The same formats (except for HIT, KWIC, and OCC) may be used
with the DISPLAY ACC command to display the record for a
specified Accession Number.

ENTER DISPLAY FORMAT (GEN):end

=> d his

(FILE 'HOME' ENTERED AT 15:45:30 ON 29 SEP 2003)

FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
15:45:38 ON 29 SEP 2003
E SCHUBERT
E E3 AND WALTER
E SCHUBERT
L1 1 S E3 AND WALTER
L2 1 S E3 AND WALTER
L3 229 S E3 AND CELL
L4 5 S L3 AND TARGET

FILE 'STNGUIDE' ENTERED AT 15:52:18 ON 29 SEP 2003
L5 0 S CELL SPECIFIC TARGET AND PROCESS
L6 0 S CELL SPECIFIC TARGET
L7 0 S CELL- SPECIFIC TARGET
L8 0 S CELL- SPECIFIC AND SCHUBERT
L9 0 S MELK
L10 4 S PROTEOMICS

=> d l10 ibib abs 1-4
'IBIB' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'
'ABS' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'

The following are valid formats:

The default display format is GEN.

GEN --- AN, DBN, DESC, PROD
DBS --- AN, DBN, DESC, SUBJ, SI, DATA, UA, PROD,
SUPP, REPR, SFIELD, PROP, DFIELD, TFIELD,
FEAT, EXAMPLE
ALL --- AN, DBN, DESC, SUBJ, CC, SI, DATA, UA, NTE,
PROD, SUPP, REPR, SFIELD, PROP, DFIELD, TFIELD,
FEAT, PRICE, EXAMPLE
COVERAGE - AN, DBN, SUBJ, CC, SI, DATA
FIELDS --- AN, DBN, SFIELD, PROP, DFIELD, TFIELD
HIT ------ All fields containing hit terms
KWIC ----- All fields containing hit terms
OCC ------ List of display fields containing hit terms

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields, enter the display field
codes. For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>). Examples of formats include: 'GEN';
'AN'; 'SI,CC'. You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, KWIC, and OCC) may be used
with the DISPLAY ACC command to display the record for a
specified Accession Number.

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ENTER DISPLAY FORMAT (GEN):end

=> d hist

     (FILE 'HOME' ENTERED AT 15:45:30 ON 29 SEP 2003)

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     15:45:38 ON 29 SEP 2003
                E SCHUBERT
                E E3 AND WALTER
                E SCHUBERT
L1            1 S E3 AND WALTER
L2            1 S E3 AND WALTER
L3          229 S E3 AND CELL
L4            5 S L3 AND TARGET

     FILE 'STNGUIDE' ENTERED AT 15:52:18 ON 29 SEP 2003
L5            0 S CELL SPECIFIC TARGET AND PROCESS
L6            0 S CELL SPECIFIC TARGET
L7            0 S CELL- SPECIFIC TARGET
L8            0 S CELL- SPECIFIC AND SCHUBERT
L9            0 S MELK
L10           4 S PROTEOMICS

=> FIL BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                1.44      36.64

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                0.00      -1.30

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FILE 'WPIDS' ENTERED AT 16:06:49 ON 29 SEP 2003
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FILE 'SCISEARCH' ENTERED AT 16:06:49 ON 29 SEP 2003
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=> d l10 abs ibib 1-4
YOU HAVE REQUESTED DATA FROM FILE 'STNGUIDE' - CONTINUE? (Y)/N:y


'ABS' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'
'IBIB' IS NOT A VALID FORMAT FOR FILE 'STNGUIDE'

The following are valid formats:

The default display format is GEN.
```

The same formats (except for HIT, KWIC, and OCC) may be used with the DISPLAY ACC command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (GEN):end

=> s proteomic?
L11 16796 PROTEOMIC?

=> s l11 and MELK
L12 1 L11 AND MELK

=> d l12 abs ibib

L12 ANSWER 1 OF 1 MEDLINE on STN
AB **MELK** is an ultrasensitive topological **proteomics** technology analysing proteins on the single cell level (Multi-Epitope-Ligand-'Kartographie'). It can trace out large scale protein patterns with subcellular resolution, mapping the topological position of many proteins simultaneously in a cell. Thereby, it addresses higher level order in a proteome, referred to as the toponome, coding cell functions by topologically and timely determined webs of interacting proteins. The resulting cellular protein maps provide new structures in the proteome: single combinatorial protein patterns (s-CPP), and combinatorial protein pattern motifs (CPP-motifs), bound to superior units. They are images of functional protein networks, which are specific signatures of tissues, cell types, cell states and diseases. The technology unravels hierarchies of proteins related to particular cell functions or dysfunctions, thus identifying and prioritising key proteins within cell and tissue protein networks. Interlocking **MELK** with the drug screening machinery provides new clues related to the selection of target proteins, and functionally relevant hits and drug leads. The present chapter summarizes the steps that have contributed to the establishment of the technology.

ACCESSION NUMBER: 2003397091 MEDLINE
DOCUMENT NUMBER: 22815613 PubMed ID: 12934931
TITLE: Topological **proteomics**, toponomics, **MELK** -technology.
AUTHOR: Schubert Walter
CORPORATE SOURCE: MelTec Ltd., ZENIT-Building, Leipziger Strasse 44, 39120 Magdeburg, Germany.. info@meltec.de
SOURCE: ADVANCES IN BIOCHEMICAL ENGINEERING/BIOTECHNOLOGY, (2003) 83 189-209. Ref: 30
Journal code: 8307733. ISSN: 0724-6145.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030826
Last Updated on STN: 20030928
Entered Medline: 20030926

=> s proteomic and process
L13 2438 PROTEOMIC AND PROCESS

=> s l13 and cultivated
L14 8 L13 AND CULTIVATED

=> d l14 ibib abs

L14 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:232833 BIOSIS
DOCUMENT NUMBER: PREV200300232833
TITLE: **Proteomic** analysis of Lactococcus lactis, a lactic acid bacterium.
AUTHOR(S): Guillot, Alain; Gitton, Christophe; Anglade, Patricia; Mistou, Michel-Yves (1)
CORPORATE SOURCE: (1) Unite de Biochimie et Structure des Proteines, Institut National de la Recherche Agronomique, 78352, Jouy-en-Josas cedex, France: mistou@jouy.inra.fr France
SOURCE: Proteomics, (March 2003, 2003) Vol. 3, No. 3, pp. 337-354. print.
ISSN: 1615-9853.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Lactococcus lactis is a Gram-positive bacteria, which belongs to the group of lactic acid bacteria among which several genera play an essential role in the manufacture of food products. Cytosolic proteins of L. lactis IL1403 **cultivated** in M17 broth have been resolved by two-dimensional gel electrophoresis using two pH gradients (pH 4-7, 4.5-5.5). More than 230 spots were identified by peptide mass fingerprints, corresponding to 25% of the predicted acid proteome. The present study made it possible to describe at the proteome level a significant number of cellular pathways (glycolysis, fermentation, nucleotide metabolism, proteolysis, fatty acid and peptidoglycan synthesis) related to important physiological **processes** and technological properties. It also indicated that the fermentative metabolism, which characterizes L. lactis is associated with a high expression of glycolytic enzymes. Thirty-four proteins were matched to open reading frames for which there is no assigned function. The comparison at the proteome level of two strains of L. lactis showed an important protein polymorphism. The comparison of the proteomes of glucose- and lactose-grown cells revealed an unexpected link between the nature of the carbon source and the metabolism of pyrimidine nucleotides.

=> d l14 ibib abs 2-8

L14 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:292643 BIOSIS
DOCUMENT NUMBER: PREV200100292643
TITLE: Genomic and **proteomic** analysis of microbial function in the gastrointestinal tract of ruminants.
AUTHOR(S): White, Bryan A. (1); Morrison, Mark
CORPORATE SOURCE: (1) Departments of Animal Sciences and Veterinary Pathobiology, and the Division of Nutritional Sciences, University of Illinois at Urbana-Champaign, 1207 West Gregory Drive, Urbana, IL, 61801: b-white2@uiuc.edu, morrison.234@osu.edu USA
SOURCE: Asian-Australasian Journal of Animal Sciences, (June, 2001) Vol. 14, No. 6, pp. 880-884. print.
ISSN: 1011-2367.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Rumen microbiology research has undergone several evolutionary steps: the isolation and nutritional characterization of readily **cultivated** microbes; followed by the cloning and sequence analysis of individual genes relevant to key digestive **processes**; through to the use of small subunit ribosomal RNA (SSU rRNA) sequences for a

cultivation-independent examination of microbial diversity. Our knowledge of rumen microbiology has expanded as a result, but the translation of this information into productive alterations of ruminal function has been rather limited. For instance, the cloning and characterization of cellulase genes in Escherichia coli has yielded some valuable information about this complex enzyme system in ruminal bacteria. SSU rRNA analyses have also confirmed that a considerable amount of the microbial diversity in the rumen is not represented in existing culture collections. However, we still have little idea of whether the key, and potentially rate-limiting, gene products and (or) microbial interactions have been identified. Technologies allowing high throughput nucleotide and protein sequence analysis have led to the emergence of two new fields of investigation, genomics and **proteomics**. Both disciplines can be further subdivided into functional and comparative lines of investigation. The massive accumulation of microbial DNA and protein sequence data, including complete genome sequences, is revolutionizing the way we examine microbial physiology and diversity. We describe here some examples of our use of genomics- and **proteomics**-based methods, to analyze the cellulase system of Ruminococcus flavefaciens FD-1 and explore the genome of Ruminococcus albus 8. At Illinois, we are using bacterial artificial chromosome (BAC) vectors to create libraries containing large (>75 kbases), contiguous segments of DNA from R. flavefaciens FD-1. Considering that every bacterium is not a candidate for whole genome sequencing, BAC libraries offer an attractive, alternative method to perform physical and functional analyses of a bacterium's genome. Our first plan is to use these BAC clones to determine whether or not cellulases and accessory genes in R. flavefaciens exist in clusters of orthologous genes (COGs). **Proteomics** is also being used to complement the BAC library/DNA sequencing approach. Proteins differentially expressed in response to carbon source are being identified by 2-D SDS-PAGE, followed by in-gel-digests and peptide mass mapping by MALDI-TOF Mass Spectrometry, as well as peptide sequencing by Edman degradation. At Ohio State, we have used a combination of functional **proteomics**, mutational analysis and differential display RT-PCR to obtain evidence suggesting that in addition to a cellulosome-like mechanism, R. albus 8 possesses other mechanisms for adhesion to plant surfaces. Genome walking on either side of these differentially expressed transcripts has also resulted in two interesting observations: i) a relatively large number of genes with no matches in the current databases and; ii) the identification of genes with a high level of sequence identity to those identified, until now, in the archaebacteria. Genomics and **proteomics** will also accelerate our understanding of microbial interactions, and allow a greater degree of in situ analyses in the future. The challenge is to utilize genomics and **proteomics** to improve our fundamental understanding of microbial physiology, diversity and ecology, and overcome constraints to ruminal function.

L14 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:244402 CAPLUS
DOCUMENT NUMBER: 139:130342
TITLE: **Proteomic** analysis of Lactococcus lactis, a lactic acid bacterium
AUTHOR(S): Guillot, Alain; Gitton, Christophe; Anglade, Patricia; Mistou, Michel-Yves
CORPORATE SOURCE: Institut National de la Recherche Agronomique, Jouy-en-Josas, Fr.
SOURCE: Proteomics (2003), 3(3), 337-354
CODEN: PROTC7; ISSN: 1615-9853
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lactococcus lactis is a Gram-pos. bacteria, which belongs to the group of

lactic acid bacteria among which several genera play an essential role in the manuf. of food products. Cytosolic proteins of L. lactis IL1403 **cultivated** in M17 broth have been resolved by two-dimensional gel electrophoresis using two pH gradients (pH 4-7, 4.5-5.5). More than 230 spots were identified by peptide mass fingerprints, corresponding to 25% of the predicted acid proteome. The present study made it possible to describe at the proteome level a significant no. of cellular pathways (glycolysis, fermn., nucleotide metab., proteolysis, fatty acid and peptidoglycan synthesis) related to important physiol. **processes** and technol. properties. It also indicated that the fermentative metab., which characterizes L. lactis is assocd. with a high expression of glycolytic enzymes. Thirty-four proteins were matched to open reading frames for which there is no assigned function. The comparison at the proteome level of two strains of L. lactis showed an important protein polymorphism. The comparison of the proteomes of glucose- and lactose-grown cells revealed an unexpected link between the nature of the carbon source and the metab. of pyrimidine nucleotides.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:398436 CAPLUS
DOCUMENT NUMBER: 136:129446
TITLE: Genomic and **proteomic** analysis of microbial function in the gastrointestinal tract of ruminants
AUTHOR(S): White, Bryan A.; Morrison, Mark
CORPORATE SOURCE: Departments of Animal Sciences and Veterinary Pathobiology, University of Illinois at Urbana-Champaign, Urbana, IL, 61801, USA
SOURCE: Asian-Australasian Journal of Animal Sciences (2001), 14(6), 880-884
CODEN: AJASEL; ISSN: 1011-2367
PUBLISHER: Asian-Australasian Journal of Animal Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Rumen microbiol. research has undergone several evolutionary steps: the isolation and nutritional characterization of readily **cultivated** microbes; followed by the cloning and sequence anal. of individual genes relevant to key digestive **processes**; through to the use of small subunit rRNA (SSU rRNA) sequences for a cultivation-independent examn. of microbial diversity. Our knowledge of rumen microbiol. has expanded as a result, but the translation of this information into productive alterations of ruminal function has been rather limited. For instance, the cloning and characterization of cellulase genes in Escherichia coli has yielded some valuable information about this complex enzyme system in ruminal bacteria. SSU rRNA analyses have also confirmed that a considerable amt. of the microbial diversity in the rumen is not represented in existing culture collections. However, we still have little idea of whether the key, and potentially rate-limiting, gene products and (or) microbial interactions have been identified. Technologies allowing high throughput nucleotide and protein sequence anal. have led to the emergence of two new fields of investigation, genomics and **proteomics**. Both disciplines can be further subdivided into functional and comparative lines of investigation. The massive accumulation of microbial DNA and protein sequence data, including complete genome sequences, is revolutionizing the way we examine microbial physiol. and diversity. We describe here some examples of our use of genomics- and **proteomics**-based methods, to analyze the cellulase system of Ruminococcus flavefaciens FD-1 and explore the genome of R. albus 8. At Illinois, we are using bacterial artificial chromosome (BAC) vectors to create libraries contg. large (>75 kbases), contiguous segments of DNA from R. flavefaciens FD-1. Considering that every bacterium is not

a candidate for whole genome sequencing, BAC libraries offer an attractive, alternative method to perform phys. and functional analyses of a bacterium's genome. Our first plan is to use these BAC clones to det. whether or not cellulases and accessory genes in R. flavefaciens exist in clusters of orthologous genes (COGs). **Proteomics** is also being used to complement the BAC library/DNA sequencing approach. Proteins differentially expressed in response to carbon source are being identified by 2-D SDS-PAGE, followed by in-gel-digests and peptide mass mapping by MALDI-TOF Mass Spectrometry, as well as peptide sequencing by Edman degrdn. At Ohio State, we have used a combination of functional **proteomics**, mutational anal. and differential display RT-PCR to obtain evidence suggesting that in addn. to a cellulosome-like mechanism, R. albus 8 possesses other mechanisms for adhesion to plant surfaces. Genome walking on either side of these differentially expressed transcripts has also resulted in two interesting observations: (i) a relatively large no. of genes with no matches in the current databases and; (ii) the identification of genes with a high level of sequence identity to those identified, until now, in the archaebacteria. Genomics and **proteomics** will also accelerate our understanding of microbial interactions, and allow a greater degree of in situ analyses in the future. The challenge is to utilize genomics and **proteomics** to improve our fundamental understanding of microbial physiol., diversity and ecol., and overcome constraints to ruminal function.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2003114020 IN-PROCESS
DOCUMENT NUMBER: 22514603 PubMed ID: 12627387
TITLE: **Proteomic** analysis of Lactococcus lactis, a lactic acid bacterium.
AUTHOR: Guillot Alain; Gitton Christophe; Anglade Patricia; Mistou Michel-Yves
CORPORATE SOURCE: Institut National de la Recherche Agronomique, Jouy-en-Josas, France.
SOURCE: Proteomics, (2003 Mar) 3 (3) 337-54.
Journal code: 101092707. ISSN: 1615-9853.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030311
Last Updated on STN: 20030311

AB Lactococcus lactis is a Gram-positive bacteria, which belongs to the group of lactic acid bacteria among which several genera play an essential role in the manufacture of food products. Cytosolic proteins of L. lactis IL1403 **cultivated** in M17 broth have been resolved by two-dimensional gel electrophoresis using two pH gradients (pH 4-7, 4.5-5.5). More than 230 spots were identified by peptide mass fingerprints, corresponding to 25% of the predicted acid proteome. The present study made it possible to describe at the proteome level a significant number of cellular pathways (glycolysis, fermentation, nucleotide metabolism, proteolysis, fatty acid and peptidoglycan synthesis) related to important physiological **processes** and technological properties. It also indicated that the fermentative metabolism, which characterizes L. lactis is associated with a high expression of glycolytic enzymes. Thirty-four proteins were matched to open reading frames for which there is no assigned function. The comparison at the proteome level of two strains of L. lactis showed an important protein polymorphism. The comparison of the proteomes of glucose- and lactose-grown cells revealed an unexpected link between the nature of the carbon source and the metabolism of pyrimidine nucleotides.

L14 ANSWER 6 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003124019 EMBASE
TITLE: **Proteomic** analysis of Lactococcus lactis, a lactic acid bacterium.
AUTHOR: Guillot A.; Gitton C.; Anglade P.; Mistou M.-Y.
CORPORATE SOURCE: Dr. M.-Y. Mistou, Inst. Natl. de la Rech. Agronomique, Unite Biochim./Struct. des Proteines, 78352 Jouy-en-Josas Cedex, France. mistou@jouy.inra.fr
SOURCE: Proteomics, (1 Mar 2003) 3/3 (337-354).
Refs: 54
ISSN: 1615-9853 CODEN: PROTC7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Lactococcus lactis is a Gram-positive bacteria, which belongs to the group of lactic acid bacteria among which several genera play an essential role in the manufacture of food products. Cytosolic proteins of L. lactis IL1403 **cultivated** in M17 broth have been resolved by two-dimensional gel electrophoresis using two pH gradients (pH 4-7, 4.5-5.5). More than 230 spots were identified by peptide mass fingerprints, corresponding to 25% of the predicted acid proteome. The present study made it possible to describe at the proteome level a significant number of cellular pathways (glycolysis, fermentation, nucleotide metabolism, proteolysis, fatty acid and peptidoglycan synthesis) related to important physiological **processes** and technological properties. It also indicated that the fermentative metabolism, which characterizes L. lactis is associated with a high expression of glycolytic enzymes. Thirty-four proteins were matched to open reading frames for which there is no assigned function. The comparison at the proteome level of two strains of L. lactis showed an important protein polymorphism. The comparison of the proteomes of glucose- and lactose-grown cells revealed an unexpected link between the nature of the carbon source and the metabolism of pyrimidine nucleotides.

L14 ANSWER 7 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2003:286319 SCISEARCH
THE GENUINE ARTICLE: 658AT
TITLE: **Proteomic** analysis of Lactococcus lactis, a lactic acid bacterium
AUTHOR: Guillot A; Gitton C; Anglade P; Mistou M Y (Reprint)
CORPORATE SOURCE: Inst Natl Rech Agron, Unite Biochim & Struct Prot, F-78352 Jouy En Josas, France (Reprint)
COUNTRY OF AUTHOR: France
SOURCE: PROTEOMICS, (MAR 2003) Vol. 3, No. 3, pp. 337-354.
Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 WEINHEIM, GERMANY.
ISSN: 1615-9853.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 54
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Lactococcus lactis is a Gram-positive bacteria, which belongs to the group of lactic acid bacteria among which several genera play an essential role in the manufacture of food products. Cytosolic proteins of L. lactis IL1403 **cultivated** in M17 broth have been resolved by two-dimensional gel electrophoresis using two pH gradients (pH 4-7, 4.5-5.5). More than 230 spots were identified by peptide mass fingerprints, corresponding to 25% of the predicted acid proteome. The

present study made it possible to describe at the proteome level a significant number of cellular pathways (glycolysis, fermentation, nucleotide metabolism, proteolysis, fatty acid and peptidoglycan synthesis) related to important physiological **processes** and technological properties. It also indicated that the fermentative metabolism, which characterizes L. lactis is associated with a high expression of glycolytic enzymes. Thirty-four proteins were matched to open reading frames for which there is no assigned function. The comparison at the proteome level of two strains of L. lactis showed an important protein polymorphism. The comparison of the proteomes of glucose- and lactose-grown cells revealed an unexpected link between the nature of the carbon source and the metabolism of pyrimidine nucleotides.

L14 ANSWER 8 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:251427 SCISEARCH
THE GENUINE ARTICLE: 413VM
TITLE: Genomic and **proteomic** analysis of microbial function in the gastrointestinal tract of ruminants - Review
AUTHOR: White B A (Reprint); Morrison M
CORPORATE SOURCE: Univ Illinois, Dept Anim Sci, 1207 W Gregory Dr, Urbana, IL 61801 USA (Reprint); Univ Illinois, Dept Anim Sci, Urbana, IL 61801 USA; Univ Illinois, Dept Vet Pathobiol, Urbana, IL 61801 USA; Univ Illinois, Div Nutrit Sci, Urbana, IL 61801 USA
COUNTRY OF AUTHOR: USA
SOURCE: ASIAN-AUSTRALASIAN JOURNAL OF ANIMAL SCIENCES, (JUN 2001) Vol. 14, No. 6, pp. 880-884.
Publisher: ASIAN-AUSTRALASIAN ASSOC ANIMAL PRODUCTION SOCIETIES, COLLEGE AGRICULTURE LIFE SCIENCES, DEPT ANIMAL SCIENCE TECHNOLOGY, SUWON 441-744, SOUTH KOREA.
ISSN: 1011-2367.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Rumen microbiology research has undergone several evolutionary steps: the isolation and nutritional characterization of readily **cultivated** microbes; followed by the cloning and sequence analysis of individual genes relevant to key digestive **processes**; through to the use of small subunit ribosomal RNA (SSU rRNA) sequences for cultivation-independent examination of microbial diversity. Our knowledge of rumen microbiology has expanded as a result, but the translation of this information into productive alterations of ruminal function has been rather limited. For instance, the cloning and characterization of cellulase genes in Escherichia coli has yielded some valuable information about this complex enzyme system in ruminal bacteria. SSU rRNA analyses have also confirmed that a considerable amount of the microbial diversity in the rumen is not represented in existing culture collections. However, we still have little idea of whether the key, and potentially rate-limiting, gene products and (or) microbial interactions have been identified. Technologies allowing high throughput nucleotide and protein sequence analysis have led to the emergence of two new fields of investigation, genomics and **proteomics**. Both disciplines can be further subdivided into functional and comparative lines of investigation. The massive accumulation of microbial DNA and protein sequence data, including complete genome sequences, is revolutionizing the way we examine microbial physiology and diversity. We describe here some examples of our use of genomics- and **proteomics**-based methods, to analyze the cellulase system of Ruminococcus flavefaciens FD-1 and explore the genome of Ruminococcus albus 8. At Illinois, we are using bacterial artificial chromosome (BAC) vectors to create libraries containing large (>75

kbases), contiguous segments of DNA from R. flavefaciens FD-1. Considering that every bacterium is nor a candidate for whole genome sequencing, BAC libraries offer an attractive, alternative method to perform physical and functional analyses of a bacterium's genome. Our first plan is to use these BAC clones to determine whether or not cellulases and accessory genes in R flavefaciens exist in clusters of orthologous genes (COGs). **Proteomics** is also being used to complement the BAC library/DNA sequencing approach. Proteins differentially expressed in response to carbon source are being identified by 2-D SDS-PAGE, followed by in-gel-digests and peptide mass mapping by MALDI-TOF Mass Spectrometry, as well as peptide sequencing by Edman degradation. At Ohio State, we have used a combination of functional **proteomics**, mutational analysis and differential display RT-PCR to obtain evidence suggesting that in addition to a cellulosome-like mechanism, R albus 8 possesses other mechanisms for adhesion to plant surfaces. Genome walking on either side of these differentially expressed transcripts has also resulted in two interesting observations: i) a relatively large number of genes with no matches in the current databases and; ii) the identification of genes with a high level of sequence identity to those identified, until now, in the archaebacteria. Genomics and **proteomics** will also accelerate our understanding of microbial interactions, and allow a greater degree of in situ analyses in the future. The challenge is to utilize genomics and **proteomics** to improve our fundamental understanding of microbial physiology, diversity and ecology, and overcome constraints to ruminal function.

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=> s l13 and cell
L15       1282 L13 AND CELL

=> s l15 and schubert
L16          0 L15 AND SCHUBERT

=> s l15 and heterogeneous
L17         15 L15 AND HETEROGENEOUS

=> d l17 ibib abs 1-15

L17  ANSWER 1 OF 15  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER:    2003:439217  BIOSIS
DOCUMENT NUMBER:     PREV200300439217
TITLE:               Proteomic analysis of human vessels: Application
                     to atherosclerotic plaques.
AUTHOR(S):           Duran, Mari Carmen; Mas, Sebastian; Martin-Ventura, Jose
                     Luis; Meilhac, Olivier; Michel, Jean Baptiste;
                     Gallego-Delgado, Julio; Lazaro, Alberto; Tunon, Jose;
                     Egido, Jesus; Vivanco, Fernando (1)
CORPORATE SOURCE:    (1) Departamento de Inmunologia, Fundacion Jimenez Diaz,
                     Avda. Reyes Catolicos 2, 28040, Madrid, Spain:
                     fvivanco@fjd.es Spain
SOURCE:              Proteomics, (June 2003, 2003) Vol. 3, No. 6, pp. 973-978.
                     print.
                     ISSN: 1615-9853.
DOCUMENT TYPE:       Article
LANGUAGE:            English
AB   Atherosclerosis is a chronic disease that affects medium and large
     arteries. This process originates from the interaction between
     cells of the arterial wall, lipoproteins and inflammatory
     cells, leading to the development of complex lesions or plaques
     that protrude into the arterial lumen. Plaque rupture and thrombosis
     result in acute clinical complications such as myocardial infarction and
     stroke. Owing to the heterogeneous cellular composition of the
```

plaques, a **proteomic** analysis of the whole lesion is not appropriate. Therefore, we have studied the proteins secreted by human carotid atherosclerotic plaques, obtained by endarterectomy. Normal artery segments and different regions of the surgical pieces (noncomplicated plaque, complicated plaque with thrombus) were cultured in protein-free medium and the secreted proteins (supernatants) analyzed by two-dimensional gel electrophoresis. Normal artery segments secreted a moderate number of proteins (42 spots). However in the two-dimensional (2-D) gels (pH 3-10) of segments bearing a plaque, the number of spots increased markedly (154). The number of spots also increased (202) in the 2-D gels of artery segments with a ruptured plaque and thrombus. Thus, the more complicated the lesion, the higher the number of secreted proteins, suggesting the production of specific proteins relating to the complexity of the atherosclerotic lesion.

L17 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:561129 BIOSIS
DOCUMENT NUMBER: PREV200200561129
TITLE: Orderly pattern of development of the autoantibody response in (New Zealand WhiteXBXSB)F1 lupus mice: Characterization of target antigens and antigen spreading by two-dimensional gel electrophoresis and mass spectrometry.
AUTHOR(S): Thebault, Sandrine; Gilbert, Daniele; Hubert, Marie; Drouot, Laurent; Machour, Nadine; Lange, Catherine; Charlionet, Roland; Tron, Francois (1)
CORPORATE SOURCE: (1) Faculte de Medecine et de Pharmacie, Institut de la Sante et de la Recherche Medicale Unite 519, 22 Boulevard Gambetta, 76183, Rouen Cedex: francois.tron@chu-rouen.fr France
SOURCE: Journal of Immunology, (October 1, 2002) Vol. 169, No. 7, pp. 4046-4053. http://www.jimmunol.org/. print. ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Immunoblots of a two-dimensional PAGE-separated HL-60 **cell** **proteomic** map and mass spectrometry were combined to characterize proteins targeted by autoantibodies produced by male (New Zealand WhiteXBXSB)F1 (WB) mice that develop lupus and anti-phospholipid syndrome. Analysis of sera sequentially obtained from seven individual mice at different ages showed that six proteins, vimentin, heat shock protein 60, UV excision-repair protein RAD23, alpha-enolase, **heterogeneous** nuclear ribonucleoprotein L, and nucleophosmin, were the targets of the B **cell** autoimmune response, and that autoantibodies to them were synthesized sequentially in an orderly pattern that recurred in all the male WB mice analyzed: anti-vimentin first and anti-nucleophosmin last, with anti-RAD23 and anti-heat shock protein 60, then anti-alpha-enolase and anti-**heterogeneous** nuclear ribonucleoprotein L Abs occuring concomitantly. Anti-vimentin reactivity always appeared before anti-cardiolipin and anti-DNA Abs, suggesting that vimentin is the immunogen initiating the autoimmune **process**. The pattern of HL-60 proteins recognized by female WB sera differed from that of male sera, indicating that the Y chromosome-linked autoimmune acceleration gene is not an accelerator but a strong modifier of the autoimmune response. Thus, 1) combining two-dimensional PAGE and mass spectrometry constitutes a powerful tool to identify the set of Ags bound by autoantibodies present in a single serum and the whole autoantibody pattern of an autoimmune disease; 2) the diversification of the autoimmune response in male WB mice occurs in a predetermined pattern consistent with Ag spreading, and thus provides a useful model to further our understanding of the development of the autoantibody response in lupus.

L17 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:530595 CAPLUS
DOCUMENT NUMBER: 139:193854
TITLE: **Proteomic** analysis of human vessels: Application to atherosclerotic plaques
AUTHOR(S): Duran, Mari Carmen; Mas, Sebastian; Martin-Ventura, Jose Luis; Meilhac, Olivier; Michel, Jean Baptiste; Gallego-Delgado, Julio; Lazaro, Alberto; Tunon, Jose; Egido, Jesus; Vivanco, Fernando
CORPORATE SOURCE: Department Immunology, Fundacion Jimenez Diaz, Madrid, Spain
SOURCE: Proteomics (2003), 3(6), 973-978
CODEN: PROTC7; ISSN: 1615-9853
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Atherosclerosis is a chronic disease that affects medium and large arteries. This **process** originates from the interaction between **cells** of the arterial wall, lipoproteins and inflammatory **cells**, leading to the development of complex lesions or plaques that protrude into the arterial lumen. Plaque rupture and thrombosis result in acute clin. complications such as myocardial infarction and stroke. Owing to the **heterogeneous** cellular compn. of the plaques, a **proteomic** anal. of the whole lesion is not appropriate. Therefore, we have studied the proteins secreted by human carotid atherosclerotic plaques, obtained by endarterectomy. Normal artery segments and different regions of the surgical pieces (noncomplicated plaque, complicated plaque with thrombus) were cultured in protein-free medium and the secreted proteins (supernatants) analyzed by two-dimensional gel electrophoresis. Normal artery segments secreted a moderate no. of proteins (42 spots). However in the two-dimensional (2-D) gels (pH 3-10) of segments bearing a plaque, the no. of spots increased markedly (154). The no. of spots also increased (202) in the 2-D gels of artery segments with a ruptured plaque and thrombus. Thus, the more complicated the lesion, the higher the no. of secreted proteins, suggesting the prodn. of specific proteins relating to the complexity of the atherosclerotic lesion.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:3180 CAPLUS
DOCUMENT NUMBER: 138:366172
TITLE: **Proteomic** analysis of the cellular proteins induced by adaptive concentrations of hydrogen peroxide in human U937 **cells**
AUTHOR(S): Seong, Je Kyung; Kim, Do Kyun; Choi, Kun Ho; Oh, Seung Hyun; Kim, Kil Soo; Lee, Seung-Sook; Um, Hong-Duck
CORPORATE SOURCE: Laboratory of Developmental Biology College of Veterinary Medicine, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Experimental and Molecular Medicine (2002), 34(5), 374-378
CODEN: EMMEF3; ISSN: 1226-3613
PUBLISHER: Korean Society of Medical Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When **cells** are first exposed to low levels of oxidative stress, they develop a resistance to a subsequent challenge of the same stress, even at higher levels. Although some protein(s) induced by oxidative stress likely mediated this adaptive response, the nature of these proteins is unknown. In this study, the total proteins extd. from human

U937 leukemia **cells** exposed to 50 .mu.M H2O2 for 24 h to induce an optimal protective response were analyzed by two-dimensional PAGE. H2O2 treatment induced elevation of level of 34 protein spots. An anal. of these spots by a matrix assocd. laser desorption/ionization time-of-flight mass spectrometry identified 28 of the H2O2-induced proteins. These include proteins involved in energy metab., translation and RNA processing, chaperoning or mediating protein folding, cellular signaling, and redox regulation, as well as a mitochondrial channel component, and an actin-bundling protein. Therefore, it appears that the cellular adaptation to oxidative stress is a complex **process**, and is accompanied by a modulation of diverse cellular functions.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:753691 CAPLUS

DOCUMENT NUMBER: 137:231236

TITLE: Orderly pattern of development of the autoantibody response in (New Zealand White .times. BXSB)F1 lupus mice: characterization of target antigens and antigen spreading by two-dimensional gel electrophoresis and mass spectrometry

AUTHOR(S): Thebault, Sandrine; Gilbert, Daniele; Hubert, Marie; Drouot, Laurent; Machour, Nadine; Lange, Catherine; Charlionet, Roland; Tron, Francois

CORPORATE SOURCE: Institut de la Sante et de la Recherche Medicale Unite 519, Faculte de Medecine et de Pharmacie, Hopital Charles-Nicolle, Rouen, 76183, Fr.

SOURCE: Journal of Immunology (2002), 169(7), 4046-4053 CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Immunoblots of a two-dimensional PAGE-sepd. HL-60 **cell proteomic** map and mass spectrometry were combined to characterize proteins targeted by autoantibodies produced by male (New Zealand White .times. BXSB)F1 (WB) mice that develop lupus and anti-phospholipid syndrome. Anal. of sera sequentially obtained from seven individual mice at different ages showed that six proteins, vimentin, heat shock protein 60, UV excision-repair protein RAD23, .alpha.-enolase, **heterogeneous** nuclear ribonucleoprotein L, and nucleophosmin, were the targets of the B **cell** autoimmune response, and that autoantibodies to them were synthesized sequentially in an orderly pattern that recurred in all the male WB mice analyzed: anti-vimentin first and anti-nucleophosmin last, with anti-RAD23 and anti-heat shock protein 60, then anti-.alpha.-enolase and anti-**heterogeneous** nuclear ribonucleoprotein L Abs occurring concomitantly. Anti-vimentin reactivity always appeared before anti-cardiolipin and anti-DNA Abs, suggesting that vimentin is the immunogen initiating the autoimmune **process**. The pattern of HL-60 proteins recognized by female WB sera differed from that of male sera, indicating that the Y chromosome-linked autoimmune acceleration gene is not an accelerator but a strong modifier of the autoimmune response. Thus, 1) combining two-dimensional PAGE and mass spectrometry constitutes a powerful tool to identify the set of Ags bound by autoantibodies present in a single serum and the whole autoantibody pattern of an autoimmune disease; 2) the diversification of the autoimmune response in male WB mice occurs in a predetd. pattern consistent with Ag spreading, and thus provides a useful model to further our understanding of the development of the autoantibody response in lupus.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2003420473 IN-PROCESS
DOCUMENT NUMBER: 22840803 PubMed ID: 12959633
TITLE: Biomarkers, validation and pharmacokinetic-pharmacodynamic modelling.
AUTHOR: Colburn Wayne; Lee Jean
CORPORATE SOURCE: MDS Pharma Services, Phoenix, Arizona, USA.
SOURCE: CLINICAL PHARMACOKINETICS, (2003) 42 (12) 997-1022. Journal code: 7606849. ISSN: 0312-5963.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030909
Last Updated on STN: 20030909

AB Four elements are crucial to successful pharmacokinetic-pharmacodynamic (PK/PD) modelling and simulation for efficient and effective rational drug development: (i) mechanism-based biomarker selection and correlation to clinical endpoints; (ii) quantification of drug and/or metabolites in biological fluids under good laboratory practices (GLP); (iii) GLP-like biomarker method validation and measurements and; (iv) mechanism-based PK/PD modelling and validation. Biomarkers can provide great predictive value in early drug development if they reflect the mechanism of action for the intervention even if they do not become surrogate endpoints. PK/PD modelling and simulation can play a critical role in this **process**. Data from genomic and **proteomics** differentiating healthy versus disease states lead to biomarker discovery and identification. Multiple genes control complex diseases via hosts of gene products in biometabolic pathways and **cell**/organ signal transduction. Pilot exploratory studies should be conducted to identify pivotal biomarkers to be used for predictive clinical assessment of disease progression and the effect of drug intervention. Most biomarkers are endogenous macromolecules, which could be measured in biological fluids. Many exist in **heterogeneous** forms with varying activity and immunoreactivity, posting challenges for bioanalysis. Reliable and selective assays could be validated under a GLP-like environment for quantitative methods. While the need for consistent reference standards and quality control monitoring during sample analysis for biomarker assays are similar to that of drug molecules, many biomarkers have special requirements for sample collection that demand a wellcoordinated team management. Bioanalytical methods should be validated to meet study objectives at various drug development stages, and possess adequate performance to quantify biochemical responses specific to the target disease progression and drug intervention. Protocol design to produce sufficient data for PK/PD modelling would be more complex than that of PK. Knowledge of mechanism from discovery and preclinical studies are helpful for planning clinical study designs in cascade, sequential, crossover or replicate mode. The appropriate combination of biomarker identification and selection, bioanalytical methods development and validation for drugs and biomarkers, and mechanism-based PK/PD models for fitting data and predicting future clinical endpoints/outcomes provide powerful insights and guidance for effective and efficient rational drug development, toward safe and efficacious medicine for individual patients.

L17 ANSWER 7 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2003305117 IN-PROCESS
DOCUMENT NUMBER: 22717145 PubMed ID: 12833522
TITLE: **Proteomic** analysis of human vessels: application to atherosclerotic plaques.
AUTHOR: Duran Mari Carmen; Mas Sebastian; Martin-Ventura Jose Luis; Meilhac Olivier; Michel Jean Baptiste; Gallego-Delgado Julio; Lazaro Alberto; Tunon Jose; Egido Jesus; Vivanco

Fernando
CORPORATE SOURCE: Department Immunology, Fundacion Jimenez Diaz, Madrid, Spain.
SOURCE: Proteomics, (2003 Jun) 3 (6) 973-8.
Journal code: 101092707. ISSN: 1615-9853.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030701
Last Updated on STN: 20030718

AB Atherosclerosis is a chronic disease that affects medium and large arteries. This **process** originates from the interaction between **cells** of the arterial wall, lipoproteins and inflammatory **cells**, leading to the development of complex lesions or plaques that protrude into the arterial lumen. Plaque rupture and thrombosis result in acute clinical complications such as myocardial infarction and stroke. Owing to the **heterogeneous** cellular composition of the plaques, a **proteomic** analysis of the whole lesion is not appropriate. Therefore, we have studied the proteins secreted by human carotid atherosclerotic plaques, obtained by endarterectomy. Normal artery segments and different regions of the surgical pieces (noncomplicated plaque, complicated plaque with thrombus) were cultured in protein-free medium and the secreted proteins (supernatants) analyzed by two-dimensional gel electrophoresis. Normal artery segments secreted a moderate number of proteins (42 spots). However in the two-dimensional (2-D) gels (pH 3-10) of segments bearing a plaque, the number of spots increased markedly (154). The number of spots also increased (202) in the 2-D gels of artery segments with a ruptured plaque and thrombus. Thus, the more complicated the lesion, the higher the number of secreted proteins, suggesting the production of specific proteins relating to the complexity of the atherosclerotic lesion.

L17 ANSWER 8 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2002489889 MEDLINE
DOCUMENT NUMBER: 22229570 PubMed ID: 12244208
TITLE: Orderly pattern of development of the autoantibody response in (New Zealand White x BXSB)F1 lupus mice: characterization of target antigens and antigen spreading by two-dimensional gel electrophoresis and mass spectrometry.
AUTHOR: Thebault Sandrine; Gilbert Daniele; Hubert Marie; Drouot Laurent; Machour Nadine; Lange Catherine; Charlionet Roland; Tron Francois
CORPORATE SOURCE: Institut de la Sante et de la Recherche Medicale Unite 519, Faculte de Medecine et de Pharmacie, Hopital Charles-Nicolle, Rouen, France.
SOURCE: JOURNAL OF IMMUNOLOGY, (2002 Oct 1) 169 (7) 4046-53.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020928
Last Updated on STN: 20021213
Entered Medline: 20021112

AB Immunoblots of a two-dimensional PAGE-separated HL-60 **cell** **proteomic** map and mass spectrometry were combined to characterize proteins targeted by autoantibodies produced by male (New Zealand White x BXSB)F(1) (WB) mice that develop lupus and anti-phospholipid syndrome. Analysis of sera sequentially obtained from seven individual mice at

different ages showed that six proteins, vimentin, heat shock protein 60, UV excision-repair protein RAD23, alpha-enolase, **heterogeneous** nuclear ribonucleoprotein L, and nucleophosmin, were the targets of the B **cell** autoimmune response, and that autoantibodies to them were synthesized sequentially in an orderly pattern that recurred in all the male WB mice analyzed: anti-vimentin first and anti-nucleophosmin last, with anti-RAD23 and anti-heat shock protein 60, then anti-alpha-enolase and anti-**heterogeneous** nuclear ribonucleoprotein L Abs occuring concomitantly. Anti-vimentin reactivity always appeared before anti-cardiolipin and anti-DNA Abs, suggesting that vimentin is the immunogen initiating the autoimmune **process**. The pattern of HL-60 proteins recognized by female WB sera differed from that of male sera, indicating that the Y chromosome-linked autoimmune acceleration gene is not an accelerator but a strong modifier of the autoimmune response. Thus, 1) combining two-dimensional PAGE and mass spectrometry constitutes a powerful tool to identify the set of Ags bound by autoantibodies present in a single serum and the whole autoantibody pattern of an autoimmune disease; 2) the diversification of the autoimmune response in male WB mice occurs in a predetermined pattern consistent with Ag spreading, and thus provides a useful model to further our understanding of the development of the autoantibody response in lupus.

L17 ANSWER 9 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999127506 MEDLINE
DOCUMENT NUMBER: 99127506 PubMed ID: 9928545
TITLE: Experimental pathology and breast cancer genetics: new technologies.
AUTHOR: Osin P; Shipley J; Lu Y J; Crook T; Gusterson B A
CORPORATE SOURCE: Section of Cell Biology and Experimental Pathology, Institute of Cancer Research, Haddow Laboratories, Sutton, Surrey, UK.
SOURCE: RECENT RESULTS IN CANCER RESEARCH, (1998) 152 35-48. Ref: 37
Journal code: 0044671. ISSN: 0080-0015.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990312

AB The goal is to understand the critical events in tumour development and to apply this understanding to new approaches to diagnosis, prevention and treatment. It is clear that breast cancer is a **heterogeneous** disease at the molecular level, raising the possibility of a future functional classification based on mechanisms rather than morphology. These molecular phenotypes will also confer predictive value on the potential of the tumour to invade, metastasise and respond to or resist new therapeutic strategies. Studies of the genome in individuals are predicted also to enable the identification of polymorphisms that are associated with increased susceptibility to environmental factors, in addition to possibly explaining de novo variations in responses to drugs and radiation. The difficulty is how to identify which, of the approximately 30,000 genes expressed by a typical cancer **cell** alone or in combination, are the ones involved in these **processes**. The majority of breast cancers have such a multitude of molecular changes that it is difficult to distinguish between those that are critical to tumour progression and those that are epiphenomena of genetic instability and abnormalities in DNA repair. The identification of the

earliest events in carcinogenesis must be the best hope, as it will then be possible to target the events that predispose to other secondary changes before they occur. Genomics and **proteomics** is the current hope to take us forward. This involves the application of a number of new technologies to facilitate the profiling of individual tumours, including laser-guided microdissection of microscopic lesions, comparative genomic hybridisation and loss of heterozygosity analysis of DNA using microarray technology to study DNA and expressed RNAs and protein profiling using 2D gel mass spectroscopy. With over 100,000 mRNAs and proteins to examine in complex tissues and in various combinations, there is obviously going to be a requirement for a large investment in computing power (bioinformatics) to facilitate the analysis of these data in relation to the clinical characteristics of the individual tumour and the patient.

L17 ANSWER 10 OF 15 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003270566 EMBASE
TITLE: **Proteomic** analysis of human vessels: Application to atherosclerotic plaques.
AUTHOR: Duran M.C.; Mas S.; Martin-Ventura J.L.; Meilhac O.; Michel J.B.; Gallego-Delgado J.; Lazaro A.; Tunon J.; Egido J.; Vivanco F.
CORPORATE SOURCE: Dr. F. Vivanco, Departamento de Inmunologia, Fundacion Jimenez Diaz, Avda. Reyes Catolicos, 2-28040-Madrid, Spain. fvivanco@fjd.es
SOURCE: Proteomics, (1 Jun 2003) 3/6 (973-978).
Refs: 18
ISSN: 1615-9853 CODEN: PROTC7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Atherosclerosis is a chronic disease that affects medium and large arteries. This **process** originates from the interaction between **cells** of the arterial wall, lipoproteins and inflammatory **cells**, leading to the development of complex lesions or plaques that protrude into the arterial lumen. Plaque rupture and thrombosis result in acute clinical complications such as myocardial infarction and stroke. Owing to the **heterogeneous** cellular composition of the plaques, a **proteomic** analysis of the whole lesion is not appropriate. Therefore, we have studied the proteins secreted by human carotid atherosclerotic plaques, obtained by endarterectomy. Normal artery segments and different regions of the surgical pieces (noncomplicated plaque, complicated plaque with thrombus) were cultured in protein-free medium and the secreted proteins (supernatants) analyzed by two-dimensional gel electrophoresis. Normal artery segments secreted a moderate number of proteins (42 spots). However in the two-dimensional (2-D) gels (pH 3-10) of segments bearing a plaque, the number of spots increased markedly (154). The number of spots also increased (202) in the 2-D gels of artery segments with a ruptured plaque and thrombus. Thus, the more complicated the lesion, the higher the number of secreted proteins, suggesting the production of specific proteins relating to the complexity of the atherosclerotic lesion.

L17 ANSWER 11 OF 15 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003130598 EMBASE
TITLE: Utility of peptide-protein affinity complexes in

proteomics: Identification of interaction partners of a tumor suppressor p21([141-160])(cip1/waf1) peptide.

AUTHOR: Gururaja T.L.; Li W.; Payan D.G.; Anderson D.C.

CORPORATE SOURCE: Dr. T.L. Gururaja, Rigel Pharmaceuticals Inc., 240 East Grand Avenue, South San Francisco, CA 94080, United States. tgururaja@rigel.com

SOURCE: Journal of Peptide Research, (1 Apr 2003) 61/4 (163-176). Refs: 65
ISSN: 1397-002X CODEN: JPERFA

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We used a N-biotinylated peptide analog of the C-terminal domain of the tumor suppressor protein, p21(cip1/waf1) to elucidate peptide/protein interacting partners. The C-terminal domain of p21(cip1/waf1) protein spanning 141-160 amino acid residues is known to bind PCNA and this interaction is important in many biological **processes** including **cell**-cycle control. This C-terminal 20-mer efficiently extracts PCNA in the presence of a variety of N- or C-terminally attached affinity tags. Using difference silver stained 2D gels combined with in-gel tryptic digests, we identified the difference spots using MALDI-TOF mass spectrometry-based peptide mass fingerprinting followed by a database search using PROFOUND against NCBIs human nonredundant protein sequence data bank. Identified spots include the p48 subunit of chromatin assembly factor-I, the heat shock 70 protein analog BiP, calmodulin, nucleolin and a spot similar in size to dimeric PCNA. In contrast, microcapillary ion-trap LC-MS/MS analysis of a tryptic digest of entire affinity extracts derived from both control and experimental runs followed by database searches using SEQUEST confirmed the presence of most of the above proteins. This strategy also identified hnRNPA1, HPSP90.alpha., HSP40 and T-complex protein 1, a protein similar to prothymosin, and a possible allelic variant of the p21(cip1/waf1) protein. The use of N-biotinylated peptide derived from the C-terminal domain of p21(cip1/waf1) protein in **proteomic** analysis exemplified here suggests that peptides obtained from intracellular functional screens could also potentially serve as efficient baits to discover new drug targets.

L17 ANSWER 12 OF 15 EMBASE on STN

ACCESSION NUMBER: 2002339598 EMBASE

TITLE: Orderly pattern of development of the autoantibody response in (New Zealand White x BXSB)F(1) lupus mice: Characterization of target antigens and antigen spreading by two-dimensional gel electrophoresis and mass spectrometry.

AUTHOR: Thebault S.; Gilbert D.; Hubert M.; Drouot L.; Machour N.; Lange C.; Charlionet R.; Tron F.

CORPORATE SOURCE: Dr. F. Tron, Inst. Sante/Rech. Medicale Unite 519, Faculte de Medecine et de Pharmacie, 22 boulevard Gambetta, 76183 Rouen Cedex, France. francois.tron@chu-rouen.fr

SOURCE: Journal of Immunology, (1 Oct 2002) 169/7 (4046-4053). Refs: 51
ISSN: 0022-1767 CODEN: JOIMA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Immunoblots of a two-dimensional PAGE-separated HL-60 **cell proteomic** map and mass spectrometry were combined to characterize proteins targeted by autoantibodies produced by male (New Zealand White x BXSB)F(1) (WB) mice that develop lupus and anti-phospholipid syndrome. Analysis of sera sequentially obtained from seven individual mice at different ages showed that six proteins, vimentin, heat shock protein 60, UV excision-repair protein RAD23, .alpha.-enolase, **heterogeneous** nuclear ribonucleoprotein L, and nucleophosmin, were the targets of the B **cell** autoimmune response, and that autoantibodies to them were synthesized sequentially in an orderly pattern that recurred in all the male WB mice analyzed: anti-vimentin first and anti-nucleophosmin last, with anti-RAD23 and anti-heat shock protein 60, then anti-.alpha.-enolase and anti-**heterogeneous** nuclear ribonucleoprotein L Abs occuring concomitantly. Anti-vimentin reactivity always appeared before anti-cardiolipin and anti-DNA Abs, suggesting that vimentin is the immunogen initiating the autoimmune **process**. The pattern of HL-60 proteins recognized by female WB sera differed from that of male sera, indicating that the Y chromosome-linked autoimmune acceleration gene is not an accelerator but a strong modifier of the autoimmune response. Thus, 1) combining two-dimensional PAGE and mass spectrometry constitutes a powerful tool to identify the set of Ags bound by autoantibodies present in a single serum and the whole autoantibody pattern of an autoimmune disease; 2) the diversification of the autoimmune response in male WB mice occurs in a predetermined pattern consistent with Ag spreading, and thus provides a useful model to further our understanding of the development of the auto-antibody response in lupus.

L17 ANSWER 13 OF 15 EMBASE on STN

ACCESSION NUMBER: 2002337436 EMBASE

TITLE: Tissue microdissection and its applications in pathology.

AUTHOR: Curran S.; Murray G.I.

CORPORATE SOURCE: G.I. Murray, Department of Pathology, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, United Kingdom. g.i.murray@abdn.ac.uk

SOURCE: Current Diagnostic Pathology, (2002) 8/3 (183-192). Refs: 42
ISSN: 0968-6053 CODEN: CDPAFN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Human tissues are composed of complex admixtures of different **cell** types. In order to examine a specific population of **cells**, it is necessary to isolate them from surrounding **cells**: this **process** can be problematic. Tissue microdissection may be defined as a **process** of isolating a morphologically distinct population of **cells** from a tissue section or cytological preparation composed of a mixture of **heterogeneous cell** types. The purpose of tissue microdissection is to provide a homogeneous sample of **cells**, in a form suitable for further analysis. Microdissection is becomingly increasingly important, due to the development of a variety of powerful molecular analytical techniques, which must be applied to samples of a high degree of purity/homogeneity in order to provide clinically and biologically meaningful results. A variety of different methods of microdissection have been developed. This review describes the basic principles of tissue microdissection techniques, and considers their applications in the field of human pathology. .COPYRGT. 2002 Elsevier Science Ltd. All rights reserved.

L17 ANSWER 14 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2003:595589 SCISEARCH
THE GENUINE ARTICLE: 697CL
TITLE: **Proteomic** analysis of human vessels: Application to atherosclerotic plaques
AUTHOR: Duran M C; Mas S; Martin-Ventura J L; Meilhac O; Michel J B; Gallego-Delgado J; Lazaro A; Tunon J; Egido J; Vivanco F (Reprint)
CORPORATE SOURCE: Fdn Jimenez Diaz, Dept Immunol, Avda Reyes Catollicos 2, Madrid 28040, Spain (Reprint); Fdn Jimenez Diaz, Dept Immunol, Madrid 28040, Spain; Autonomous Univ Madrid, Renal & Vasc Lab, Fdn Jimenez Diaz, E-28049 Madrid, Spain; CHU Xavier Bichat, Unit 460 INSERM, Paris, France; Fdn Jimenez Diaz, Dept Cardiol, E-28040 Madrid, Spain; Univ Complutense, Preteom Unit, Dept Biochem & Mol Biol 1, E-28040 Madrid, Spain
COUNTRY OF AUTHOR: Spain; France
SOURCE: PROTEOMICS, (JUN 2003) Vol. 3, No. 6, pp. 973-978. Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 WEINHEIM, GERMANY. ISSN: 1615-9853.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 18

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Atherosclerosis is a chronic disease that affects medium and large arteries. This **process** originates from the interaction between **cells** of the arterial wall, lipoproteins and inflammatory **cells**, leading to the development of complex lesions or plaques that protrude into the arterial lumen. Plaque rupture and thrombosis result in acute clinical complications such as myocardial infarction and stroke. Owing to the **heterogeneous** cellular composition of the plaques, a **proteomic** analysis of the whole lesion is not appropriate. Therefore, we have studied the proteins secreted by human carotid atherosclerotic plaques, obtained by endarterectomy. Normal artery segments and different regions of the surgical pieces (noncomplicated plaque, complicated plaque with thrombus) were cultured in protein-free medium and the secreted proteins (supernatants) analyzed by two-dimensional gel electrophoresis. Normal artery segments secreted a moderate number of proteins (42 spots). However in the two-dimensional (2-D) gels (pH 3-10) of segments bearing a plaque, the number of spots increased markedly (154). The number of spots also increased (202) in the 2-D gels of artery segments with a ruptured plaque and thrombus. Thus, the more complicated the lesion, the higher the number of secreted proteins, suggesting the production of specific proteins relating to the complexity of the atherosclerotic lesion.

L17 ANSWER 15 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2002:815911 SCISEARCH
THE GENUINE ARTICLE: 598QV
TITLE: Orderly pattern of development of the autoantibody response in (New Zealand White x BXSB)F-1 lupus mice: Characterization of target antigens and antigen spreading by two-dimensional gel electrophoresis and mass spectrometry
AUTHOR: Thebault S; Gilbert D; Hubert M; Drouot L; Machour N; Lange C; Charlionet R; Tron F (Reprint)
CORPORATE SOURCE: Inst Sante & Rech, Med Unite 519, Fac Med & Pharm, 22 Blvd Gambetta, F-76183 Rouen, France (Reprint); Hop Charles Nicolle, Inst Sante & Rech, Med Unit 519, Fac Med & Pharm, Rouen, France; Inst Rech Chim Organ Fine, Lab Spect, Inst

Fed Rech Multidisciplinaires Peptides, Rouen, France
COUNTRY OF AUTHOR: France
SOURCE: JOURNAL OF IMMUNOLOGY, (1 OCT 2002) Vol. 169, No. 7, pp. 4046-4053.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 51

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Immunoblots of a two-dimensional PAGE-separated HL-60 **cell proteomic** map and mass spectrometry were combined to characterize proteins targeted by autoantibodies produced by male (New Zealand White X BXSB)F-1 (WB) mice that develop lupus and anti-phospholipid syndrome. Analysis of sera sequentially obtained from seven individual mice at different ages showed that six proteins, vimentin, heat shock protein 60, UV excision-repair protein RAD23, alpha-enolase, **heterogeneous** nuclear ribonucleoprotein L, and nucleophosmin, were the targets of the B **cell** autoimmune response, and that autoantibodies to them were synthesized sequentially in an orderly pattern that recurred in all the male WB mice analyzed: anti-vimentin first and anti-nucleophosmin last, with anti-RAD23 and anti-heat shock protein 60, then anti-alpha-enolase and anti-**heterogeneous** nuclear ribonucleoprotein L Abs occuring concomitantly. Anti-vimentin reactivity always appeared before anti-cardiolipin and anti-DNA Abs, suggesting that vimentin is the immunogen initiating the autoimmune **process**. The pattern of HL-60 proteins recognized by female WB sera differed from that of male sera, indicating that the Y chromosome-linked autoimmune acceleration gene is not an accelerator but a strong modifier of the autoimmune response. Thus, 1) combining two-dimensional PAGE and mass spectrometry constitutes a powerful tool to identify the set of Ags bound by autoantibodies present in a single serum and the whole autoantibody pattern of an autoimmune disease; 2) the diversification of the autoimmune response in male WB mice occurs in a predetermined pattern consistent with Ag spreading, and thus provides a useful model to further our understanding of the development of the autoantibody response in lupus.

```
=> s l15 and protein chips
L18          1 L15 AND PROTEIN CHIPS

=> d l18 abs

L18  ANSWER 1 OF 1  WPIDS  COPYRIGHT 2003 THOMSON DERWENT on STN
AN   2003-175091 [17]   WPIDS
CR   2003-183869 [18]
AB   WO 200294454 A UPAB: 20030317
     NOVELTY - Fabrication of microdevices involves a vapor deposition coating
     process, where the coating includes functional groups having an
     intrinsic reactivity to react with target molecules.
          DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a
     microdevice article for separation of biomolecules in an electrical field
     comprising a polymeric coating for capturing molecules at the surface,
     which bind at least a part of the biomolecules subjected to screening,
     only temporarily allowing their subsequent release.
          USE - For parallel analysis of biomolecules (particularly hydrogels,
     polyelectrolytes or temp-sensitive molecules) and for separation of
     biomolecules in an electrical field (all claimed). The biomolecules
     include biologically active molecules in pharmaceutical technology such as
     in the fields of drug discovery, proteomics, genomics,
     high-throughput screening, clinical diagnostics, and other applications
```

such as manufacturing of **cell** arrays, immobilization of drugs for tissue engineering, microreactors, surfaces for protein and DNA screening and on electro-optical devices e.g. miniaturized analytical systems, biomedical devices, tools for chemistry and biochemistry and systems for fundamental research; such as useful for decoltation of implantable devices e.g. heart valves, pacemakers, stents, embolization coils, bone substitution, hip substitution, bone screws, vascular grafts etc.; improved scaffold for tissue engineering, plates for in vitro **cell** culture, resins for protein synthesis, microchip based diagnostic screening, protein purification, DNA purification, DNA chips, **protein chips**, arrays of quantum dots, electro-optical devices, and coating of three-dimensional structures such as membranes, micro-reactors, micro-channels, foams, scaffold etc. The functionalized coating can be used for microdevices made of different materials such as polymers, composites, silicon, semiconductors, glass or metal.

ADVANTAGE - The **process** is a simple one-step **process** to prepare high-content and high-throughput screening surfaces and can be quickly scaled-up. The polymer interfaces are highly reactive and contain chemical groups having intrinsic reactivity to react with target molecules, in which, at least part of capturing molecules specifically bind to biomolecules that are subject to screening, in binding pairs such as antibody/antigen, antibody/hapten, enzyme/substrate, integrin/extracellular matrix component, biomolecule/**cell**, **cell**/**cell**, carrier protein/substrate, lectine/carbohydrate, protein/carbohydrate, carbohydrate/carbohydrate, **cell** adhesion molecule/**cell** surface receptor, receptor/hormone, receptor/cytokine, protein/DNA, protein/RNA, peptide/DNA, two DNA single strains, DNA/RNA, DNA/DNA, in which either of both partners of the couples serve as capturing molecules. The use of capturing molecules avoids the step of surface modification of the bulk material. The coating **process** provides an increased surface concentration of functional groups with a defined and controlled ratio, compared to conventional methods such as plasma treatment. Due to chemically stable background of the deposited polymer, aging effects as a consequence of interactions with analyte solutions can be reduced or ruled out. Due to the mild character of the deposition **process**, side reactions are suppressed and the deposited films are homogenous with respect to their chemical structure and topology. Gradients in the functionalized groups in the coatings can also be produced by establishment of temperature gradients at the substrate subjected to coating. Straightforward synthesis achieves spatially directed immobilization of biomolecules. The once deposited film can be subjected to further modification using conventional methods. The coating step is substrate independent, thus provides a generic approach to microstructuring of microdevices. The method provides unique characteristics of various instantly reacting functional groups, a defined and chemically stable polymer base layer with defined properties, non-degradability, the possibility to create activity gradients, and the feasibility for patterning. The method overcomes the restrictions associated with gold/alkanethiolates-based techniques such as surface modification of the bulk material and side reactions including the fabrication or incorporation of potently harmful chemicals prior to immobilization, and previous deposition of gold, the method maintains the intrinsic advantages of soft lithography e.g. accuracy, broad availability and low costs. The manufacture of the microdevices by soft lithography, allows easy scale-up by replication, involving replica molding comprising casting of prepolymer against a master and preparing a negative replica of the master in polydiemethylsiloxane The coating can be produced in any shape ranging from three dimensional to porous structure.

Dwg.0/0

=> d l18 abs ibib

L18 ANSWER 1 OF 1 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2003-175091 [17] WPIDS
CR 2003-183869 [18]
AB WO 200294454 A UPAB: 20030317
NOVELTY - Fabrication of microdevices involves a vapor deposition coating **process**, where the coating includes functional groups having an intrinsic reactivity to react with target molecules.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a microdevice article for separation of biomolecules in an electrical field comprising a polymeric coating for capturing molecules at the surface, which bind at least a part of the biomolecules subjected to screening, only temporarily allowing their subsequent release.

USE - For parallel analysis of biomolecules (particularly hydrogels, polyelectrolytes or temp-sensitive molecules) and for separation of biomolecules in an electrical field (all claimed). The biomolecules include biologically active molecules in pharmaceutical technology such as in the fields of drug discovery, **proteomics**, genomics, high-throughput screening, clinical diagnostics, and other applications such as manufacturing of **cell** arrays, immobilization of drugs for tissue engineering, microreactors, surfaces for protein and DNA screening and on electro-optical devices e.g. miniaturized analytical systems, biomedical devices, tools for chemistry and biochemistry and systems for fundamental research; such as useful for decoltation of implantable devices e.g. heart valves, pacemakers, stents, embolization coils, bone substitution, hip substitution, bone screws, vascular grafts etc.; improved scaffold for tissue engineering, plates for in vitro **cell** culture, resins for protein synthesis, microchip based diagnostic screening, protein purification, DNA purification, DNA chips, **protein chips**, arrays of quantum dots, electro-optical devices, and coating of three-dimensional structures such as membranes, micro-reactors, micro-channels, foams, scaffold etc. The functionalized coating can be used for microdevices made of different materials such as polymers, composites, silicon, semiconductors, glass or metal.

ADVANTAGE - The **process** is a simple one-step **process** to prepare high-content and high-throughput screening surfaces and can be quickly scaled-up. The polymer interfaces are highly reactive and contain chemical groups having intrinsic reactivity to react with target molecules, in which, at least part of capturing molecules specifically bind to biomolecules that are subject to screening, in binding pairs such as antibody/antigen, antibody/hapten, enzyme/substrate, integrin/extracellular matrix component, biomolecule/**cell**, **cell**/**cell**, carrier protein/substrate, lectine/carbohydrate, protein/carbohydrate, carbohydrate/carbohydrate, **cell** adhesion molecule/**cell** surface receptor, receptor/hormone, receptor/cytokine, protein/DNA, protein/RNA, peptide/DNA, two DNA single strains, DNA/RNA, DNA/DNA, in which either of both partners of the couples serve as capturing molecules. The use of capturing molecules avoids the step of surface modification of the bulk material. The coating **process** provides an increased surface concentration of functional groups with a defined and controlled ratio, compared to conventional methods such as plasma treatment. Due to chemically stable background of the deposited polymer, aging effects as a consequence of interactions with analyte solutions can be reduced or ruled out. Due to the mild character of the deposition **process**, side reactions are suppressed and the deposited films are homogenous with respect to their chemical structure and topology. Gradients in the functionalized groups in the coatings can also be produced by establishment of temperature gradients at the substrate subjected to coating. Straightforward synthesis achieves spatially directed immobilization of biomolecules. The once deposited film can be subjected

to further modification using conventional methods. The coating step is substrate independent, thus provides a generic approach to microstructuring of microdevices. The method provides unique characteristics of various instantly reacting functional groups, a defined and chemically stable polymer base layer with defined properties, non-degradability, the possibility to create activity gradients, and the feasibility for patterning. The method overcomes the restrictions associated with gold/alkanethiolates-based techniques such as surface modification of the bulk material and side reactions including the fabrication or incorporation of potently harmful chemicals prior to immobilization, and previous deposition of gold, the method maintains the intrinsic advantages of soft lithography e.g. accuracy, broad availability and low costs. The manufacture of the microdevices by soft lithography, allows easy scale-up by replication, involving replica molding comprising casting of prepolymer against a master and preparing a negative replica of the master in polydiemethylsiloxane The coating can be produced in any shape ranging from three dimensional to porous structure.

Dwg.0/0

ACCESSION NUMBER: 2003-175091 [17] WPIDS
CROSS REFERENCE: 2003-183869 [18]
DOC. NO. NON-CPI: N2003-137926
DOC. NO. CPI: C2003-045709
TITLE: Fabrication of microdevices for parallel analysis of biomolecules involves a vapor deposition coating **process** with the coating including functional groups having an intrinsic reactivity to react with target molecules.
DERWENT CLASS: A26 A89 B04 D16 M13 P42 S03
INVENTOR(S): LAHANN, J
PATENT ASSIGNEE(S): (LAHA-I) LAHANN J
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002094454	A1	20021128	(200317)*	EN	16

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

DE 10124873 A1 20021205 (200317)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002094454	A1	WO 2002-US16326	20020522
DE 10124873	A1	DE 2001-10124873	20010522

PRIORITY APPLN. INFO: DE 2001-10125872 20010522; DE 2001-10124873 20010522

=> s l15 and automatic?
L19 4 L15 AND AUTOMATIC?

=> d l19 abs ibib 1-4

L19 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

AB The objective of this paper is to present a methodol. for developing and calibrating models of complex reaction/transport systems. In particular, the complex network of biochem. reaction/transport **processes** and their spatial organization make the development of a predictive model of a living **cell** a grand challenge for the 21st century. However, advances in reaction/transport modeling and the exponentially growing databases of genomic, **proteomic**, metabolic, and bioelec. data make **cell** modeling feasible, if these two elements can be **automatically** integrated in an unbiased fashion. In this paper, we present a procedure to integrate data with a new **cell** model, Karyote, that accounts for many of the phys. **processes** needed to attain the goal of predictive modeling. Our integration methodol. is based on the use of information theory. The model is integrated with a variety of types and qualities of exptl. data using an objective error assessment approach. Data that can be used in this approach include NMR, spectroscopy, microscopy, and elec. potentiometry. The approach is demonstrated on the well-studied Trypanosoma brucei system. A major obstacle for the development of a predictive **cell** model is that the complexity of these systems makes it unlikely that any model presently available will soon be complete in terms of the set of **processes** accounted for. Thus, one is faced with the challenge of calibrating and running an incomplete model. We present a probability functional method that allows the integration of exptl. data and soft information such as choice of error measure, a priori information, and phys. motivated regularization to address the incompleteness challenge.

ACCESSION NUMBER: 2003:726762 CAPLUS

TITLE: Toward Automated **Cell** Model Development through Information Theory

AUTHOR(S): Sayyed-Ahmad, A.; Tuncay, K.; Ortoleva, Peter J.

CORPORATE SOURCE: Center for Cell and Virus Theory Department of Chemistry, Indiana University, Bloomington, IN, 47405, USA

SOURCE: Journal of Physical Chemistry ACS ASAP
CODEN: JPCHAX; ISSN: 0022-3654

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

AB When presented with a mixt. of intact proteins, electrospray ionization with Fourier-transform mass spectrometry (ESI-FTMS) has the capability to obtain direct fragmentation information from isolated ions. However, the automation of this capability has not been achieved to date. We have developed software for unattended acquisition of protein tandem mass spectrometry (MS/MS) data and batch processing of the resulting files for identification of whole proteins. Mixts. of both protein stds. (8-29 kDa) and Methanococcus jannaschii cytosolic proteins (up to six components < 20 kDa) were infused via an autosampler, and MS/MS data were acquired without human intervention. The acquisition software recognizes ESI charge state patterns, generates protein-specific isolation waveforms on-the-fly, and fragments ions using two different IR laser times. In addn. to protein stds., five wild-type proteins (7-14 kDa) were identified **automatically** with 100% sequence coverage from the M. jannaschii database. The software underpins a measurement platform for sample-dependent acquisition of MS/MS data for whole proteins, a crit. step to realize **proteomics** with 100% sequence coverage in a higher throughput setting.

ACCESSION NUMBER: 2002:785182 CAPLUS

DOCUMENT NUMBER: 138:85921

TITLE: Fourier-transform mass spectrometry for automated fragmentation and identification of 5-20 kda proteins in mixtures

AUTHOR(S): Johnson, Jeffrey R.; Meng, Fanyu; Forbes, Andrew J.; Cargile, Benjamin J.; Kelleher, Neil L.

CORPORATE SOURCE: Department of Chemistry, University of Illinois, Urbana, IL, USA

SOURCE: Electrophoresis (2002), 23(18), 3217-3223
CODEN: ELCTDN; ISSN: 0173-0835

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 4 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-371684 [35] WPIDS

AB WO2003011553 A UPAB: 20030603

NOVELTY - Preparation of an artificial **cell** membrane (A) by dispensing a membrane lipid (I) across an aperture then thinning (I) by applying suction at the sides.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for producing a membrane (A') in which a liquid polymer is used in place of (I) and heat is applied to (II) before, during or after some stage in the **process**; and

(2) an apparatus for preparing (A) or (A') comprising a member with at least one aperture and at least one adjacent side channel for applying suction.

USE - (A), including bilayer lipid membranes, are useful e.g. in ion-channel sensing; DNA sensors; **proteomics** and design/synthesis of proteins. Also arrays of (A) on a chip are useful for classifying and assaying agents for their effects on cellular receptors and to improve characterization of pathogens. Polymeric membranes prepared similarly are useful as fluid filters.

ADVANTAGE - The method is suitable for automated production of membranes that retain stability and integrity without a cellular infrastructure, without requiring cumbersome techniques such as the patch clamp method. The status of the membrane can be monitored continuously during use and any damaged membranes can be regenerated **automatically**. When used in conjunction with in vitro translation/transcription systems, complex membrane-bound receptor systems can be formed, optionally with reagents drawn, electrically, to specific sites, allowing control over which proteins are expressed form a large array. This makes possible simultaneous analysis of many complex molecular combinations without interference from extraneous components (as happens in cellular systems).

DESCRIPTION OF DRAWING(S) - Schematic diagram of the apparatus for preparing membranes, and the stages involved in lipid membrane formation (BLM = bilayer lipid membrane).

Dwg.3/34

ACCESSION NUMBER: 2003-371684 [35] WPIDS

DOC. NO. CPI: C2003-098539

TITLE: Preparation of artificial **cell** or polymeric membranes, useful e.g. as DNA sensors, prepared by applying suction to a solution across an opening.

DERWENT CLASS: A89 B04 D16

INVENTOR(S): PARAMESWARAN, L; YOUNG, A

PATENT ASSIGNEE(S): (MASI) MASSACHUSETTS INST TECHNOLOGY

COUNTRY COUNT: 100

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2003011553 A1 20030213 (200335)* EN 50
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003062657 A1 20030403 (200335)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003011553 A1		WO 2002-US24266	20020730
US 2003062657 A1	Provisional	US 2001-309259P	20010731
		US 2002-209321	20020730

PRIORITY APPLN. INFO: US 2001-309259P 20010731; US 2002-209321 20020730

L19 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB Two-dimensional electrophoresis is a widely used method for separating a large number of proteins from complex protein mixtures and for revealing differential patterns of protein expressions. In the computer-assisted proteome research, the comparison of protein separation profiles involves several heuristic steps, ranging from protein spot detection to matching of unknown spots. An important prerequisite for efficient protein spot matching is the image warping step, where the geometric relationship between the gel profiles is modeled on the basis of a given set of known corresponding spots, so-called landmarks, and the locations of unknown spots are predicted using the optimized model. Traditionally, polynomial functions together with least squares optimization has been used, even though this approach is known to be incapable of modeling all the complex distortions inherent in electrophoretic data. To satisfy the need of more flexible gel distortion correction, a hierarchical grid transformation method with stochastic optimization is presented. The method provides an adaptive multiresolution model between the gels, and good correction performance in the practical crossvalidation tests suggests that **automatic** warping of gel images could be based on this approach. We believe that the proposed model also has significance in the ultimate comparison of corresponding protein spots since the matching **process** should benefit from the closeness of the true spot pairs.

ACCESSION NUMBER: 2002442751 EMBASE
TITLE: Hierarchical grid transformation for image warping in the analysis of two-dimensional electrophoresis gels.
AUTHOR: Salmi J.; Aittokallio T.; Westerholm J.; Griese M.; Rosengren A.; Nyman T.A.; Lahesmaa R.; Nevalainen O.
CORPORATE SOURCE: Dr. T. Aittokallio, Turku Centre for Computer Science, Lemminkaisenkatu 14A, FIN-20520 Turku, Finland. tero.aittokallio@utu.fi
SOURCE: Proteomics, (1 Nov 2002) 2/11 (1504-1515). Refs: 21
ISSN: 1615-9853 CODEN: PROTC7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        118.55     163.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
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LAST RELOADED: Sep 26, 2003 (20030926/UP).

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FULL ESTIMATED COST                                          0.42     163.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                          0.00      -5.86

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=> d hist

     (FILE 'HOME' ENTERED AT 15:45:30 ON 29 SEP 2003)

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     15:45:38 ON 29 SEP 2003
                E SCHUBERT
                E E3 AND WALTER
                E SCHUBERT
L1            1 S E3 AND WALTER
L2            1 S E3 AND WALTER
L3          229 S E3 AND CELL
L4            5 S L3 AND TARGET

     FILE 'STNGUIDE' ENTERED AT 15:52:18 ON 29 SEP 2003
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L5              0 S CELL SPECIFIC TARGET AND PROCESS
L6              0 S CELL SPECIFIC TARGET
L7              0 S CELL- SPECIFIC TARGET
L8              0 S CELL- SPECIFIC AND SCHUBERT
L9              0 S MELK
L10             4 S PROTEOMICS

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     16:06:49 ON 29 SEP 2003

     FILE 'STNGUIDE' ENTERED AT 16:07:16 ON 29 SEP 2003

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     16:07:32 ON 29 SEP 2003
L11         16796 S PROTEOMIC?
L12             1 S L11 AND MELK
L13          2438 S PROTEOMIC AND PROCESS
L14             8 S L13 AND CULTIVATED
L15          1282 S L13 AND CELL
L16             0 S L15 AND SCHUBERT
L17            15 S L15 AND HETEROGENEOUS
L18             1 S L15 AND PROTEIN CHIPS
L19             4 S L15 AND AUTOMATIC?

     FILE 'STNGUIDE' ENTERED AT 16:21:29 ON 29 SEP 2003

     FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS, EMBASE, SCISEARCH' ENTERED AT
     16:25:49 ON 29 SEP 2003

=> s l15 and endotheli?
L20           27 L15 AND ENDOTHELI?

=> dup rem l20
PROCESSING COMPLETED FOR L20
L21            16 DUP REM L20 (11 DUPLICATES REMOVED)

=> d l21 1-16 abs ibib

L21  ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2003 ACS on STN
AB   Genomic actions and/or proteomic interactions for pathophysiol.
     processes and for physiol. processes are detd. at
     assocd. redox state conditions.  Protein interactions are correlated with
     oxygen tensions.  Identification of markers for disease including epitopes
     is effected in the presence of simulated redox state perturbations.
     Screening for previously unknown receptors and activating ligands is
     carried out in the presence of alteration of redox state.
ACCESSION NUMBER:         2003:300520  CAPLUS
DOCUMENT NUMBER:          138:283690
TITLE:                    Determination of proteomic interaction and
                          genomic action in the presence of associated redox
                          state conditions and physiological, pathophysiological
                          and drug screening applications
INVENTOR(S):              Stamler, Jonathan S.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 9 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
```

US 2003073088	A1	20030417	US 2001-977693	20011016
WO 2003033721	A2	20030424	WO 2002-US31571	20021015
WO 2003033721	A3	20030814		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-977693 A 20011016

L21 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1

AB Atherosclerosis is a progressive and complex pathophysiological **process** occurring in large arteries. Although it is of multifactorial origin, the disease develops at preferential sites along the vasculature in regions experiencing specific hemodynamic conditions that are predisposed to **endothelial** dysfunction. The exact mechanisms allowing **endothelial cells** to discriminate between plaque-free and plaque-prone flows remain to be explored. To investigate such mechanisms, we performed a **proteomic** analysis on **endothelial cells** exposed in vitro to these two-flow patterns. A few spots on the two-dimensional gel had an intensity that was differentially regulated by plaque-free versus plaque-prone flows. One of them was further investigated and identified as macrophage-capping protein (Cap G), a member of the gelsolin protein superfamily. A 2-fold increase of Cap G protein and a 5-fold increase of Cap G mRNA were observed in **cells** exposed to a plaque-free flow as compared with static cultures. This increase was not observed in **cells** exposed to plaque-prone flow. Plaque-free flow induced a corresponding increase in nuclear and cytoskeletal-associated Cap G. Finally, overexpression of Cap G in transfection assays increased the motility potential of **endothelial cells**. These observations together with the known functions of Cap G suggest that Cap G may contribute to the protective effect exerted by plaque-free flow on **endothelial cells**. On the contrary, in **cells** exposed to a plaque-prone flow, no induction of Cap G expression could be observed.

ACCESSION NUMBER: 2003:444600 BIOSIS
DOCUMENT NUMBER: PREV200300444600
TITLE: Cap G, a gelsolin family protein modulating protective effects of unidirectional shear stress.
AUTHOR(S): Pellieux, Corinne; Desgeorges, Alain; Pigeon, Christelle Haziza; Chambaz, Celine; Yin, Helen; Hayoz, Daniel; Silacci, Paolo (1)
CORPORATE SOURCE: (1) Division of Hypertension and Vascular Medicine, Centre Hospitalier Universitaire Vaudois, 1015, Lausanne, Switzerland: paolo.silacci@epfl.ch Switzerland
SOURCE: Journal of Biological Chemistry, (August 1 2003) Vol. 278, No. 31, pp. 29136-29144. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

L21 ANSWER 3 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB Cancer development is driven by the accumulation of DNA changes in the approximately 40 000 chromosomal genes. In solid tumours, chromosomal numerical/structural aberrations are common. DNA repair defects may lead to genome-wide genetic instability, which can drive further cancer progression. The genes code the actual players in the cellular **processes**, the 100 000-10 million proteins, which in (pre)malignant **cells** can also be altered in a variety of ways. Over the past decade, our knowledge of the human genome and Genomics (the study of the human genome) in (pre)malignancies has increased enormously and **Proteomics** (the analysis of the protein complement of the genome) has taken off as well. Both will play an increasingly important role. In this article, a short description of the essential molecular biological **cell processes** is given. Important genomic and **proteomic** research methods are described and illustrated. Applications are still limited, but the evidence so far is exciting. Will genomics replace classical diagnostic or prognostic procedures? In breast cancers, the gene expression array is stronger than classical criteria, but in endometrial hyperplasia, quantitative morphological features are more cost-effective than genetic testing. It is still too early to make strong statements, the more so because it is expected that genomics and **proteomics** will expand rapidly. However, it is likely that they will take a central place in the understanding, diagnosis, monitoring and treatment of (pre)cancers of many different sites.

ACCESSION NUMBER: 2003201384 EMBASE
TITLE: Genomics and **proteomics** in cancer.
AUTHOR: Baak J.P.A.; Path F.R.C.; Hermsen M.A.J.A.; Meijer G.; Schmidt J.; Janssen E.A.M.
CORPORATE SOURCE: J.P.A. Baak, Department of Pathology, Central Hospital for Rogaland, Box 8001, 4068 Stavanger, Norway. baja@sir.no
SOURCE: European Journal of Cancer, (2003) 39/9 (1199-1215). Refs: 112
ISSN: 0959-8049 CODEN: EJCAEL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L21 ANSWER 4 OF 16 SCISEARCH
AB Blood platelets are important components of haemostasis. After their activation they cause healing of wounds by forming plugs and initiate repair **processes**. One important event in regulating this activation is the phosphorylation/dephosphorylation of multiple proteins on various tyrosine, serine and threonine residues. To understand the exact molecular mechanisms in platelet activation it is essential to identify proteins involved in the signalling pathways and to localise and characterise their phosphorylation sites. After treatment with P-32 and separation by 2D-PAGE using different pI ranges, phosphorylated platelet proteins were detected by autoradiography. Phosphotyrosine-containing proteins were assigned by immunoblotting with an anti-phosphotyrosine antibody. Another approach for the identification of phosphorylated proteins was immunoprecipitation of tyrosine-phosphorylated proteins using an anti-phosphotyrosine antibody. Protein spots/bands of interest were excised from the get, digested with trypsin and analysed by MALDI-TOF-MS and nano-LC-ESI-MS/MS, respectively. Several phosphorylated proteins could be identified and the localisation of some in vivo phosphorylation sites was possible.
ACCESSION NUMBER: 2003:772136 SCISEARCH
THE GENUINE ARTICLE: 718PL
TITLE: Differential analysis of phosphorylated proteins in

resting and thrombin-stimulated human platelets
AUTHOR: Marcus K (Reprint); Moebius J; Meyer H E
CORPORATE SOURCE: Ruhr Univ Bochum, Med Proteom Ctr, ZKF 141, Univ Str 150, D-44780 Bochum, Germany (Reprint); Ruhr Univ Bochum, Med Proteom Ctr, ZKF 141, D-44780 Bochum, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: ANALYTICAL AND BIOANALYTICAL CHEMISTRY, (AUG 2003) Vol. 376, No. 7, pp. 973-993.
Publisher: SPRINGER-VERLAG BERLIN, HEIDELBERGER PLATZ 3, D-14197 BERLIN, GERMANY.
ISSN: 1618-2642.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 96
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AB The **endothelium** is a single layer of **cells** lining the inside face of all blood vessels. It constitutes a major metabolic organ which is critically involved in the generation and the regulation of multiple physiological and pathological **processes** such as coagulation, hemostasis, inflammation, atherosclerosis, angiogenesis and cancerous metastasis dissemination. In order to increase our knowledge about the protein content and the main biological pathways of human vascular **endothelial cells**, we have undertaken the **proteomic** analysis of the most explored present **endothelial cell** model, i.e. primo-cultures of human umbilical vein **endothelial cells** (HUVECs). Using low levels of protein loads (apprx30 mug), the association of two-dimensional electrophoresis with matrix-assisted laser desorption/ionization-time of flight mass spectrometry, liquid chromatography-tandem mass spectrometry and database interrogations allowed us to identify 53 proteins of suspected **endothelial** origin in quiescent HUVECs. Beside cytoskeletal proteins such as actin, tubulin, tropomyosin and vimentin, we identified various proteins more especially implicated in cellular motility and plasticity (e.g. cofilin, F-actin capping protein and prefoldin), in regulation of apoptosis and senescence (protease inhibitor 9, glucose related proteins, heat shock proteins, thioredoxin peroxidase, nucleophosmin) as well as other proteins implicated in coagulation (annexin V, high mobility group protein), antigen presentation (valosin containing protein and ubiquitin carboxyl terminal hydrolase isozyme L1) and enzymatic capabilities (glutathione-S-transferase, protein disulfide isomerases, lactate deshydrogenase).
ACCESSION NUMBER: 2003:329994 BIOSIS
DOCUMENT NUMBER: PREV200300329994
TITLE: **Proteomic** study of human umbilical vein **endothelial cells** in culture.
AUTHOR(S): Bruneel, Arnaud (1); Labas, Valerie; Mailloux, Agnes; Sharma, Sanjiv; Vinh, Joelle; Vaubourdolle, Michel; Baudin, Bruno
CORPORATE SOURCE: (1) Service de Biochimie A, Hopital Saint-Antoine, AP-HP, 184 Rue du Faubourg Saint-Antoine, 75571, Paris Cedex 12, France: arnaud.bruneel@sat.ap-hop-paris.fr France
SOURCE: Proteomics, (May 2003, 2003) Vol. 3, No. 5, pp. 714-723. print.
ISSN: 1615-9853.
DOCUMENT TYPE: Article
LANGUAGE: English

L21 ANSWER 6 OF 16 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB Homeostasis of the intracellular ionic concentration, in particular

that of hydrogen ions, is pivotal to the maintenance of **cell** function and viability. Nonetheless, pH fluctuations in both the intracellular and the extracellular compartments can occurr during development, in physiological **processes** and in disease. The influence of pH variations on gene expression has been studied in different model systems, but only for a limited number of genes. We have performed a broad range analysis of the patterns of gene expression in normal human dermal fibroblasts at two different pH values (in the presence and in the absence of serum), with the aim of getting a deeper insight into the regulation of the transcriptional program as a response to a pH change. Using the Affymetrix gene chip system, we found that the expression of 2068 genes (out of 12 565) was modulated by more than two-fold at 24, 48 or 72 h after the shift of the culture medium pH to a more acidic value, stanniocalcin 1 being a remarkable example of a strongly up-regulated gene. Genes displaying a modulated pattern of expression included, among others, **cell** cycle regulators (consistent with the observation that acidic pH abolishes the growth of fibroblasts in culture) and relevant extracellular matrix (ECM) components. Extracellular matrix protein 2, a protein with a restricted pattern of expression in adult human tissues, was found to be remarkably overexpressed as a consequence of serum starvation. Since ECM components, whose expression is controlled by pH, have been used as targets for biomolecular intervention, we have complemented the Affymetrix analysis with a two-dimensional polyacrylamide gel electrophoresis analysis of proteins which are differentially secreted by fibroblasts at acidic or basic pH. Mass spectrometric analysis of more than 650 protein spots allowed the identification of 170 protein isoforms or fragments, belonging to 40 different proteins. Some proteins were only expressed at basic pH (including, for instance, tetranectin), while others (e.g., agrin) were only detectable at acidic pH. Some of the identified proteins may represent promising candidate targets for biomedical applications, e.g., for antibody-mediated vascular targeting strategies.

ACCESSION NUMBER: 2003:465783 SCISEARCH
THE GENUINE ARTICLE: 679TA
TITLE: Modulation of gene expression by extracellular pH variations in human fibroblasts: A transcriptomic and **proteomic** study
AUTHOR: Bumke M A; Neri D (Reprint); Elia G
CORPORATE SOURCE: Swiss Fed Inst Technol, Inst Pharmaceut Sci, Winterthurerstr 190, CH-8057 Zurich, Switzerland (Reprint); Swiss Fed Inst Technol, Inst Pharmaceut Sci, CH-8057 Zurich, Switzerland
COUNTRY OF AUTHOR: Switzerland
SOURCE: PROTEOMICS, (MAY 2003) Vol. 3, No. 5, pp. 675-688. Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 WEINHEIM, GERMANY. ISSN: 1615-9853.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 79
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 7 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB Several new PLA(2)s have been identified based on their nucleotide gene sequences. They were classified mainly into three groups: cytosolic PLA(2) (cPLA(2)), secretary PLA(2) (sPLA(2)), and intracellular PLA(2) (iPLA(2)). They differ from each other in terms of substrate specificity, Ca(2+) requirement and lipid modification. The questions that still remain to be addressed are the subcellular localization and differential regulation of the isoforms in various **cell** types and under different physiological conditions. It is required to identify the downstream events

that occur upon PLA(2) activation, particularly target protein or metabolic pathway for liberated arachidonic acid or other fatty acids. Understanding the same will greatly help in the development of potent and specific pharmacological modulators that can be used for basic research and clinical applications. The information of the human and other genomes of PLA(2)s, combined with the use of **proteomics** and genetically manipulated mouse models of different diseases, will illuminate us about the specific and potentially overlapping roles of individual phospholipases as mediators of physiological and pathological **processes**. Hopefully, such understanding will enable the development of specific agents aimed at decreasing the potential contribution of individual secretary phospholipases to vascular diseases. The signaling cascades involved in the activation of cPLA(2) by mitogen activated protein kinases (MAPKs) is now evident. It has been demonstrated that p44 MAPK phosphorylates cPLA(2) and increases its activity in **cells** and tissues. The phosphorylation of cPLA(2) at ser505 occurs before the increase in intracellular Ca(2+) that facilitate the binding of the lipid binding domain of cPLA(2) to phospholipids, promoting its translocation to cellular membranes and AA release. Recently, a negative feed back loop for cPLA(2) activation by MAPK has been proposed. If PLA(2) activation in a given model depends on PKC, PKA, cAMP, or MAPK then inhibition of these phosphorylating enzymes may alter activities of PLA(2) isoforms during cellular injury. Understanding the signaling pathways involved in the activation/deactivation of PLA(2) during cellular injury will point to key events that can be used to prevent the cellular injury. Furthermore, to date, there is limited information available regarding the regulation of iPLA(2) or sPLA(2) by these pathways.

ACCESSION NUMBER: 2003192191 EMBASE
TITLE: Phospholipase A(2) isoforms: A perspective.
AUTHOR: Chakraborti S.
CORPORATE SOURCE: S. Chakraborti, Dept. of Biochemistry and Biophysics, University of Kalyani, Kalyani 741235, West Bengal, India. s_chakraborti@hotmail.com
SOURCE: Cellular Signalling, (1 Jul 2003) 15/7 (637-665).
Refs: 325
ISSN: 0898-6568 CODEN: CESIEY
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L21 ANSWER 8 OF 16 EMBASE
on STN

AB A number of high resolution two-dimensional electrophoresis (2-DE) reference maps for bovine tissues and biological fluids have been determined for animals in basal state. Among the 1863 distinct protein features detected in samples of liver, kidney, muscle, plasma and red blood **cells**, 509 species were identified and associated to 209 different genes. Difficulties in the identification were related to the poorly characterized Bos taurus genome and were solved by a combined matrix-assisted laser desorption/ionisation-mass spectrometry and liquid chromatography-electrospray ionization tandem mass spectrometry approach. The experimental output allowed us to establish a 2-DE database accessible through the World Wide Web network at the URL address (http://www.iabbam.na.cnr.it/Biochem). These reference maps may serve as a tool in future veterinary medical studies aimed at the evaluation of changes in protein repertoire for altered animal physiological conditions and infectious diseases, to the definition of molecular markers for novel diagnostic kits and vaccines, as well as the characterization of protein

modifications in bovine materials following technological **processes** used in the food industry.

ACCESSION NUMBER: 2003156060 EMBASE
TITLE: Proteins from bovine tissues and biological fluids: Defining a reference electrophoresis map for liver, kidney, muscle, plasma and red blood **cells**.
AUTHOR: Talamo F.; D'Ambrosio C.; Arena S.; Del Vecchio P.; Ledda L.; Zehender G.; Ferrara L.; Scaloni A.
CORPORATE SOURCE: Dr. A. Scaloni, Proteomics/Mass Spectrom. Laboratory, I.S.P.A.A.M., National Research Council, via Argine 1085, 80147 Naples, Italy. a.scaloni@iabbam.na.cnr.it
SOURCE: Proteomics, (1 Apr 2003) 3/4 (440-460).
Refs: 40
ISSN: 1615-9853 CODEN: PROTC7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L21 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
AB An increase in permeability of the blood-brain barrier is a crit. event in the pathophysiol. **process** of multiple sclerosis and other neurodegenerative diseases. Tumor necrosis factor .alpha. (TNF.alpha.) is known to play a crucial role in this **process** and is a powerful activator of **endothelial cell** inflammatory responses. Although many reports describe effects of TNF.alpha. activation in **endothelial cells**, the mol. mechanisms specific for activation of cerebral **endothelial cells** remains unclear. The objective of this study was to identify potential pharmaceutical targets for the treatment of multiple sclerosis using mol. profiling techniques. Gene expression measurements (Affymetrix Hu6800 oligonucleotide arrays) and **proteomics** (two-dimensional gel electrophoresis and mass spectrometry) were applied to analyze early alterations in human cerebral **endothelial cells** (HCEC) activated by TNF.alpha.. Human umbilical vein **endothelial cells** (HUVEC) were used as the ref. system. The results presented show that HCEC and HUVEC respond similarly with respect to **cell** adhesion mols., chemotaxis, apoptosis and oxidative stress mols. However, nuclear factors NFkB1 and NFkB2, plasminogen activator inhibitor 1 and cofilin 1 are examples of cerebral specific responses. Our results indicate involvements of the urokinase plasminogen activator system and cytoskeletal rearrangements unique to TNF.alpha. activation of cerebral **endothelial cells**.

ACCESSION NUMBER: 2003:567392 CAPLUS
TITLE: Gene and protein expression profiling of human cerebral **endothelial cells** activated with tumor necrosis factor-.alpha.
AUTHOR(S): Franzen, Bo; Duvefelt, Kristina; Jonsson, Carina; Engelhardt, Britta; Ottervald, Jan; Wickman, Monica; Yang, Yang; Schuppe-Koistinen, Ina
CORPORATE SOURCE: CNS & Pain Control, Molecular Sciences, Gene and Protein Technology, Local Discovery Research Area, AstraZeneca R&D, Soedertaelje, Swed.
SOURCE: Molecular Brain Research (2003), 115(2), 130-146
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

L21 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB Tumor microenvironmental factors, possibly from angiogenic

processes, alter **endothelial cell** surface protein expression. Accessible to the circulation, the tumor vascular **endothelium** is a logical target for drug or gene delivery. Transcytotic vesicles (caveolae) on the surface of the **endothelium** provide a pathway for overcoming the **endothelial cell** barrier for delivery to underlying tumor **cells**. We purified luminal **endothelial cell** plasma membranes and its caveolae directly from normal and tumor-bearing tissues and resolved the membrane proteins by SDS-PAGE and 2D gel electrophoresis to reveal extensive heterogeneity of **cell** surface protein expression between tissues as well as apparent tumor-induced markers. Mass spectrometry and database searching provided key sequences of tryptic peptides of tumor-associated targets. Using antibodies to the appropriate specific polypeptides, we have confirmed the tumor-induction of the proteins. One of the tumor-induced proteins, designated TE3, is expressed in **endothelial** caveolae of solid tumors but not normal organs. Biodistribution analysis and whole body imaging (gamma scintigraphy) using TE3 antibody injected IV show the accessibility of TE3 with significant and selective tumor tissue accumulation in just 1 hour. Targeting the **endothelium** and its caveolae are worthy strategies for tumor targeting in vivo.

ACCESSION NUMBER: 2003:401903 BIOSIS
DOCUMENT NUMBER: PREV200300401903
TITLE: **Proteomic** mapping of tumor neovasculature in vivo for specific targeting and imaging of solid tumors.
AUTHOR(S): Oh, Phil (1); Subbiah, Krishnan; Testa, Jacqueline; Czarny, Malgorzata; Smith, Traci; Hearn, Kally; Wempren, Alexina; Schnitzer, Melinda; Schnitzer, Jan E.
CORPORATE SOURCE: (1) Vascular Biology, Sidney Kimmel Cancer Center, 10835 Altman Row, San Diego, CA, 92121, USA: poh@skcc.org, ksubbiah@skcc.org, jtesta@skcc.org, mczarny@skcc.org, tsmith@skcc.org, khearn@skcc.org, awempren@skcc.org, mschnitzer@skcc.org, jschnitzer@skcc.org USA
SOURCE: FASEB Journal, (March 2003, 2003) Vol. 17, No. 4-5, pp. Abstract No. 171.9. http://www.fasebj.org/. e-file. Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome San Diego, CA, USA April 11-15, 2003 FASEB . ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L21 ANSWER 11 OF 16 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-657552 [70] WPIDS
CR 2001-607180 [69]
AB WO 200263412 A UPAB: 20030214
NOVELTY - Observations are provided for the members of multiple objects allocated to pre-existing categories. Properties of latent classes are estimated from the distinguishable sets of latent classes associated with the members of objects and corresponding to the pre-existing categories.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) object classification method;
(2) computer implemented latent class identification method;
(3) method of identifying genes linked to cellular phenotype;
(4) method of identifying gene linked to metastatic properties of cancer;
(5) method of screening a drug;
(6) method of identifying genes linked to a disease of interest;
(7) membership rule generation method;
(8) method of identifying a gene linked to metastatic properties of tumor;

(9) method of identifying genes of known and unknown functions; and
(10) object image analyzing method.

USE - For identifying latent class for analysis of large amount of information for sequence analysis, gene expression and **proteomics** in the field of biology and for identification of genes linked to diseases such as leukemias such as acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic erythroleukemia chronic leukemia, chronic myelocytic leukemia, chronic lymphocytic leukemia, polycythemia vera, lymphoma, Hodgkin's disease, non-Hodgkin's disease, multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, solid tumors sarcomas, carcinomas including fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, **endotheliosarcoma**, lymphangiosarcoma, Kaposi's sarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous **cell** carcinoma, basal **cell** carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal **cell** carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, uterine cancer, testicular tumor, lung carcinoma, small **cell** lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, ependymoma, craniopharyngioma, medulloblastoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma and other types of tumors including virally induced cancers and for identification of disabilities, undesirable interactions between medications, co-morbidities, laboratory results and clinical characteristics linked to **processes** of aging, disease, cancer, diabetes, pregnancy or other clinical or pathological conditions in humans.

ADVANTAGE - Incorportes explanatory models with intentionally weak structural assumptions to prevent the imposition of artificial patterns on the data and thereby makes the models useful for complex data exploration. Estimates broad expression patterns over genes and over **cell** or tissue samples and allows quantitative determination of new biological knowledge. Assigns individual gene probabilities of membership in specific patterns and allows the quantity uncertainty associated with the allocating elements among sets of interpretable categories. Enables to conduct formal hypothesis testing, evaluate whether an identified gene pattern is different from the null hypothesis pattern and incorporates complex model structures used to exploit external biological knowledge.

DESCRIPTION OF DRAWING(S) - The figure shows the serum stimulation patterns including median estimates and 95% confidence intervals from analysis of serum stimulated fibroblasts, demonstrating both time-dependent increases and decreases in gene expression, as represented by positive and negative expression patterns.

Dwg.1/16

ACCESSION NUMBER:	2002-657552 [70] WPIDS
CROSS REFERENCE:	2001-607180 [69]
DOC. NO. NON-CPI:	N2002-519853
DOC. NO. CPI:	C2002-184535
TITLE:	Latent classes identification method for identifying genes, involves estimating properties of latent classes from distinguishable sets of latent classes associated with members of objects allocated to pre-existing categories.
DERWENT CLASS:	B04 D16 T01
INVENTOR(S):	LAZARIDIS, E
PATENT ASSIGNEE(S):	(LAZA-I) LAZARIDIS E; (UYSF-N) UNIV SOUTH FLORIDA
COUNTRY COUNT:	97

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002063412	A2	20020815	(200270)*	EN	81
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
US 2002169730	A1	20021114	(200277)		
US 2003023385	A1	20030130	(200311)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002063412	A2	WO 2001-US26672	20010828
US 2002169730	A1	WO 2001-US3616	20010205
		US 2001-940878	20010829
US 2003023385	A1	WO 2001-US3616	20010205
		US 2001-913498	20010816

PRIORITY APPLN. INFO: WO 2001-US3616 20010205

L21 ANSWER 12 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB The prognosis of hepatocellular carcinoma (HCC) still remains dismal, although many advances in its clinical study have been made. It is important for tumor control to identify the factors that predispose patients to death. With new discoveries in cancer biology, the pathological and biological prognostic factors of HCC have been studied quite extensively. Analyzing molecular markers (biomarkers) with prognostic significance is a complementary method. A large number of molecular factors have been shown to associate with the invasiveness of HCC, and have potential prognostic significance. One important aspect is the analysis of molecular markers for the cellular malignancy phenotype. These include alterations in DNA ploidy, cellular proliferation markers (PCNA, Ki-67, Mcm2, MIB1, MIA, and CSE1L/CAS protein), nuclear morphology, the p53 gene and its related molecule MDM2, other **cell** cycle regulators (cyclin A, cyclin D, cyclin E, cdc2, p27, p73), oncogenes and their receptors (such as ras, c-myc, c-fms, HGF, c-met, and erb-B receptor family members), apoptosis related factors (Fas and FasL), as well as telomerase activity. Another important aspect is the analysis of molecular markers involved in the **process** of cancer invasion and metastasis. Adhesion molecules (E-cadherin, catenins, serum intercellular adhesion molecule-1, CD44 variants), proteinases involved in the degradation of extracellular matrix (MMP-2, MMP-9, uPA, uPAR, PAI), as well as other molecules have been regarded as biomarkers for the malignant phenotype of HCC, and are related to prognosis and therapeutic outcomes. Tumor angiogenesis is critical to both the growth and metastasis of cancers including HCC, and has drawn much attention in recent years. Many angiogenesis-related markers, such as vascular **endothelial** growth factor (VEGF), basic fibroblast growth factor (bFGF), platelet-derived **endothelial cell** growth factor (PD-ECGF), thrombospondin (TSP), angiogenin, pleitrophin, and endostatin (ES) levels, as well as intratumor microvessel density (MVD) have been evaluated and found to be of prognostic significance. Body fluid (particularly blood and urinary) testing for biomarkers is easily accessible and useful in clinical patients. The prognostic significance of

circulating DNA in plasma or serum, and its genetic alterations in HCC are other important trends. More attention should be paid to these two areas in future. As the progress of the human genome project advances, so does a clearer understanding of tumor biology, and more and more new prognostic markers with high sensitivity and specificity will be found and used in clinical assays. However, the combination of some items, i. e., the pathological features and some biomarkers mentioned above, seems to be more practical for now.

ACCESSION NUMBER: 2002230965 EMBASE
TITLE: The prognostic molecular markers in hepatocellular carcinoma.
AUTHOR: Qin L.-X.; Tang Z.-Y.
CORPORATE SOURCE: Prof. Dr. Z.-Y. Tang, Liver Cancer Institute, Zhongshan Hospital, Fudan University, 136 Yi Xue Yuan Road, Shanghai 200032, China. zytang@srcap.stc.sh.cn
SOURCE: World Journal of Gastroenterology, (2002) 8/3 (385-392). Refs: 119
ISSN: 1007-9327 CODEN: WJGAF2
COUNTRY: China
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 048 Gastroenterology
016 Cancer
029 Clinical Biochemistry
005 General Pathology and Pathological Anatomy
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

L21 ANSWER 13 OF 16 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB Protein-protein interactions play crucial roles in biological **processes**. Experimental methods have been developed to survey the proteome for interacting partners and some computational approaches have been developed to extend the impact of these experimental methods. Computational methods are routinely applied to newly discovered genes to infer protein function and plausible protein-protein interactions. Here, we develop and extend a quantitative method that identifies interacting proteins based upon the correlated behavior of the evolutionary histories of protein ligands and their receptors. We have studied six families of ligand-receptor pairs including: the syntaxin/Unc-18 family, the GPCR/G-alpha's, the TGF-beta/TGF-beta receptor system, the immunity/colicin domain collection from bacteria, the chemokine/chemokine receptors, and the VEGF/VEGF receptor family. For correlation scores above a defined threshold, we were able to find an average of 79% of all known binding partners. We then applied this method to find plausible binding partners for proteins with uncharacterized binding specificities in the syntaxin/Unc-18 protein and TGF-beta/TGF-beta receptor families. Analysis of the results shows that co-evolutionary analysis of interacting protein families can reduce the search space for identifying binding partners by not only finding binding partners for uncharacterized proteins but also recognizing potentially new binding partners for previously characterized proteins. We believe that correlated evolutionary histories provide a route to exploit the wealth of whole genome sequences and recent systematic **proteomic** results to extend the impact of these studies and focus experimental efforts to categorize physiologically or pathologically relevant protein-protein interactions. (C) 2002 Elsevier Science Ltd. All rights reserved.

ACCESSION NUMBER: 2002:986433 SCISEARCH
THE GENUINE ARTICLE: 620JP
TITLE: Co-evolutionary analysis reveals insights into protein-protein interactions
AUTHOR: Goh C S; Cohen F E (Reprint)
CORPORATE SOURCE: Univ Calif San Francisco, Program Biol & Med Informat, San

Francisco, CA 94143 USA (Reprint); Univ Calif San Francisco, Dept Cellular & Mol Pharmacol, San Francisco, CA 94143 USA; Univ Calif San Francisco, Dept Biochem & Biophys, San Francisco, CA 94143 USA

COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (15 NOV 2002) Vol. 324, No. 1, pp. 177-192.
Publisher: ACADEMIC PRESS LTD ELSEVIER SCIENCE LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.
ISSN: 0022-2836.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 79

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 14 OF 16 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-589807 [66] WPIDS
AB WO 200162965 A UPAB: 20011113

NOVELTY - Differential expression screening to identify a genetic element involved in a cellular **process** (CP), involves comparing gene expressions in two **cells** (C1 and C2), where C2 has altered levels of a biological molecule implicated in CP, and identifying a genetic element whose expression differs, where gene expression in C1 or C2 is compared under different environmental conditions related to CP.

DETAILED DESCRIPTION - Differential expression screening for identifying a genetic element involved in a cellular **process**, involves comparing gene expression in (C1) and gene expression in (C2), where C2 comprises altered levels, relative to physiological levels, of a biological molecule implicated in the cellular **process**, due to the introduction of a heterologous nucleic acid directing expression of a polypeptide, into C2 and identifying a genetic element whose expression differs, where gene expression in C1 or C2 is compared under at least two different environmental conditions relevant to the cellular **process**.

INDEPENDENT CLAIMS are also included for the following:

(1) differential expression screening for identifying a gene product involved in a disease **process**, involving comparing gene expression in C1 and C2, and comparing gene expression in C1 and a third **cell** of interest (C3) that comprises altered levels, relative to physiological levels, of a candidate gene product, due to the introduction of a heterologous nucleic acid directing expression of the candidate gene product into C1, and selecting those candidate gene products which give rise to an alteration in the levels of expression of a second gene product in C3 relative to C1, where the second gene product also has altered levels of expression in C2 relative to C1; and

(2) increasing the sensitivity of differential expression screening in which gene expression of C1 and C2 in response to two different levels of a signal are compared, by introducing a heterologous nucleic acid into C1 or C2 to increase the level of a biological molecule which modulates the response of the **cell** to the signal.

USE - The method is useful for differential expression screening of a genetic element involved in a cellular **process** (claimed). The method is also useful for identifying mutations and polymorphisms that affect the biological response to a particular cellular **process**. The method also allows the molecular dissection of biological pathways by altering a particular pathway under study.

ADVANTAGE - The method is an improved screening technique based on differential expression of genes, and allows the identification of other elements that are associated with genes that are implicated in a particular cellular **process**. By influencing the level of a particular biological molecule that is implicated in the pathway under study, through the introduction of the heterologous nucleic acid into one

cell population, the method allows a pathway to be dissected into its precise molecular components.
Dwg.0/12

ACCESSION NUMBER: 2001-589807 [66] WPIDS
DOC. NO. CPI: C2001-174860
TITLE: Screening a genetic element involved in a cellular **process**, comprises comparing gene expressions in a **cell**, and a second **cell** that has altered levels of genes used in the **process**, and detecting an element with varied expression.
DERWENT CLASS: B04 D16
INVENTOR(S): KINGSMAN, A J
PATENT ASSIGNEE(S): (OXFO-N) OXFORD BIOMEDICA UK LTD
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001062965	A2	20010830	(200166)*	EN	103

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001033937	A	20010903	(200202)		
EP 1257663	A2	20021120	(200301)	EN	

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

CN 1425075	A	20030618	(200358)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001062965	A2	WO 2001-GB758	20010222
AU 2001033937	A	AU 2001-33937	20010222
EP 1257663	A2	EP 2001-905973	20010222
		WO 2001-GB758	20010222
CN 1425075	A	CN 2001-808359	20010222

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001033937	A	Based on	WO 2001062965
EP 1257663	A2	Based on	WO 2001062965

PRIORITY APPLN. INFO: GB 2000-18679 20000728; GB 2000-4197 20000222

L21 ANSWER 15 OF 16 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB The advances in **cell** culture engineering science have played a major role in the rapid expansion of mammalian **cell**-based products in the last decade. The host **cell** lines frequently used in manufacturing have converged to only a few species. For some, the genome has been completely sequenced. For others, the genomic sequence of closely related species is available, or will soon be available. The genomic and **proteomic** research tools enable one to globally survey the alterations at mRNA and protein levels to discover both primary and collateral gene expression changes and to unveil their regulation. Undoubtedly, a better understanding of these cellular **processes**

at the molecular level will lead to a better strategy for "designing" producing **cells** and for **process** optimization. Herein the genomic and **proteomic** tools are briefly reviewed and their impact on **cell** culture Engineering is discussed.

ACCESSION NUMBER: 2001:530691 SCISEARCH
THE GENUINE ARTICLE: 447FA
TITLE: Genomic and **proteomic** approaches in mammalian **cell** culture technology
AUTHOR: Korke R; Hu W S (Reprint)
CORPORATE SOURCE: Univ Minnesota, Dept Chem Engn & Mat Sci, 421 Washington Ave SE, Minneapolis, MN 55455 USA (Reprint); Univ Minnesota, Dept Chem Engn & Mat Sci, Minneapolis, MN 55455 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF THE CHINESE INSTITUTE OF CHEMICAL ENGINEERS, (MAY 2001) Vol. 32, No. 3, pp. 213-218.
Publisher: CHINESE INST CHEMICAL ENGINEER, NATL TSING HUA UNIV, HSINCHU, DEPT CHEMICAL ENGINEERING, TAIPEI 300, TAIWAN.
ISSN: 0368-1653.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 57
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L21 ANSWER 16 OF 16 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB Hepatic stellate **cell** activation is a complex **process**. Paradoxes and controversies include the origin(s) of hepatic stellate **cells**, the regulation of membrane receptor signaling and transcription, and the fate of the **cells** once liver injury resolves. Major themes have emerged, including the dominance of autocrine signaling and the identification of counterregulatory stimuli that oppose key features of activated **cells**. Advances in analytical methods including **proteomics** and gene array, coupled with powerful bioinformatics, promise to revolutionize how we view cellular responses. Our understanding of stellate **cell** activation is likely to benefit from these advances, unearthing modes of regulating cellular behavior that are not even conceivable on the basis of current paradigms.

ACCESSION NUMBER: 2000:546388 SCISEARCH
THE GENUINE ARTICLE: 333RN
TITLE: Fibrogenesis I. New insights into hepatic stellate **cell** activation: the simple becomes complex
AUTHOR: Eng F J; Friedman S L (Reprint)
CORPORATE SOURCE: CUNY MT SINAI SCH MED, DEPT MED, DIV LIVER DIS, BOX 1123, 1425 MADISON AVE, RM 1170F, NEW YORK, NY 10029 (Reprint); CUNY MT SINAI SCH MED, DEPT MED, DIV LIVER DIS, NEW YORK, NY 10029
COUNTRY OF AUTHOR: USA
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L1: Entry 15 of 19 File: USPT Apr 24, 2001

US-PAT-NO: 6221592
DOCUMENT-IDENTIFIER: US 6221592 B1

TITLE: Computer-based methods and systems for sequencing of individual nucleic acid molecules

DATE-ISSUED: April 24, 2001

INVENTOR-INFORMATION:

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US-CL-CURRENT: 435/6; 435/91.1

CLAIMS:

What is claimed is:

1. A method for imaging a single labeled nucleotide on an individual double stranded nucleic acid molecule, comprising:

(a) nicking a double stranded nucleic acid molecule elongated and fixed onto a surface so that the double stranded nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of a labeled nucleotide creating a nicked strand;

(b) enzymatically adding a single nucleotide comprising a label; and

(c) imaging the added label.

2. The method of claim 1, in which the step of nicking the double stranded nucleic acid molecule is performed by the enzyme DNase.

3. The method of claim 1, in which the surface is a planar surface.

4. The method of claim 1, in which the step of adding nucleotides comprising a label is performed by a polymerase.

5. The method of claim 4, in which the polymerase is DNA Polymerase I, the Klenow fragment of DNA Polymerase I lacking the 5'-3' exonuclease activity, T7 Sequenase v. 2.0 or Taq polymerase.

6. The method of claim 1, in which the step of imaging the label is performed using a camera and a microscope.

7. The method of claim 6, in which the step of imaging the label further comprises using laser illumination.

8. The method of claim 1, in which the step of imaging further comprises using a computer.

9. The method of claim 1, further comprising analyzing the image using a mathematical algorithm.

10. The method of claim 9, in which the mathematical algorithm is a Bayesian estimation method.

11. The method of claim 1, further comprising the steps:

(a) modifying the label after imaging the label in order to visualize the subsequently added labeled nucleotides; and

(b) repeating the steps of enzymatically adding a nucleotide comprising a label, imaging the label, and modifying the label to image multiple, consecutively added nucleotides.

12. The method of claim 11, further comprising enzymatically displacing the nicked strand of the nucleic acid molecule.

13. The method of claim 12, in which enzymatically displacing the nicked strand is performed using the Klenow fragment of DNA Polymerase I.

14. The method of claim 11, further comprising enzymatically opening the nicked sites on the double stranded nucleic acid molecule.

15. The method of claim 14, in which the step of opening the nicked sites is performed by an enzyme having 5'-3' exonuclease activity.

16. The method of claim 15, in which the enzyme having 5'-31 exonuclease activity is DNA Polymerase I or T7 exonuclease.

17. The method of claim 11, in which the label is photolabile.

18. The method of claim 11, in which the step of modifying the label after imaging is performed by photobleaching or photolysis.

19. A method for determining the nucleotide sequence of an individual double stranded nucleic acid molecule, comprising:

(a) nicking a double stranded nucleic acid molecule elongated and fixed onto a surface so that the double stranded nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of labeled nucleotides forming a 3' terminus to create an extended strand;

(b) extending the strand by adding at least one nucleotide comprising a label to the 3' terminus of the nicked site; and

(c) imaging the added label.

20. The method of claim 19, in which the step of nicking the double stranded nucleic acid molecule is performed by the enzyme DNase.

21. The method of claim 19, further comprising enzymatically displacing the nicked strand of the nucleic acid molecule.

22. The method of claim 21, in which enzymatically displacing the nicked strand is performed using the Klenow fragment of DNA Polymerase I.

23. The method of claim 19, further comprising opening the nicked sites on the double stranded nucleic acid molecule.

24. The method of claim 23, in which the step of opening the nicked sites on the double stranded nucleic acid molecule is performed by an enzyme having 5'-3' exonuclease activity.

25. The method of claim 24, in which the enzyme having 5'-3' exonuclease activity is DNA Polymerase I or T7 exonuclease.

26. The method of claim 19, in which the step of extending the strand by adding a nucleotide comprising a label is performed by a polymerase.

27. The method of claim 26, in which the polymerase is DNA Polymerase I, the Klenow fragment of DNA Polymerase I lacking the 5'-3' exonuclease activity, T7 Sequenase v. 2.0, or a Taq polymerase.

28. The method of claim 23, in which the step of opening the nicked sites on the double stranded nucleic acid molecule and extending the strand by adding a nucleotide comprising a label is performed by T7 exonuclease gene 6 and T7 Sequenase v. 2.0, respectively.

29. The method of claim 19, in which the step of imaging the label is performed using a camera and a microscope.

30. The method of claim 29, in which the step of imaging the label further comprises using laser illumination.

31. The method of claim 19, in which the label is photolabile.

32. The method of claim 19, further comprising modifying the label after imaging in order to visualize subsequently added labels.

33. The method of claim 3, in which the step of modifying the label after imaging is performed by photobleaching or photolysis.

34. The method of claim 19, in which the nucleotides comprise a mix of labeled and unlabeled nucleotides.

35. A system for determining the nucleotide sequence of an individual double stranded nucleic acid molecule, comprising:

(a) the double stranded nucleic acid molecule elongated and fixed onto a surface so that the nucleic acid molecule remains accessible for enzymatic reactions and/or hybridization reactions;

(b) a polymerase fixed on the surface;

(c) nucleotides comprising a label fixed on the surface; and

(d) a device for imaging the label to produce an image.

36. The system of claim 35, in which the polymerase is DNA Polymerase I, the Klenow fragment of DNA Polymerase I without the 5'-3' exonuclease activity T7 Sequenase v. 2.0, or Taq polymerase.

37. The system of claim 35, further comprising a nucleic acid nicking enzyme.

38. The system of claim 36, in which the nicking enzyme is a DNase.

39. The system of claim 35, in which the label is a fluorescent label.

40. The system of claim 35, further comprising a nick opening enzyme fixed on the surface.

41. The system of claim 40, in which the nick opening enzyme is T7 exonuclease gene 6, DNA Polymerase I, the Klenow fragment of DNA Polymerase I or a 5'-3'

exonuclease.

42. The system of claim 35, in which the device for imaging comprises a fluorescence microscope, a camera and a source of illumination.

43. The system of claim 35, in which the source of illumination is a laser.

44. The system of claim 35, in which the device for imaging the label processes the image using Bayesian estimation, comprising:

(a) accumulating signals of an addition site of the image;

(b) filtering the signals according to fluorescence intensity;

(c) correlating the signals with the backbone of the nucleic acid molecule;

(d) tabulating addition sites of the image using Bayesian inference estimation of the signals; and

(e) aligning and assembling the addition sites to determine a nucleotide addition.

45. A method of determining the nucleotide sequence of an individual nucleic acid molecule, comprising:

(a) exposing a nucleic acid molecule annealed with at least one primer elongated and fixed onto a surface so that the nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of labeled nucleotides to a polymerase and dideoxy nucleotides comprising a base and a label; and

(b) imaging the labeled nucleotides added onto the primer;

to determine the nucleotide sequence of the nucleic acid molecule by the addition of the labeled dideoxy nucleotide.

46. A method of determining the nucleotide sequence of an individual nucleic acid molecule, comprising:

(a) exposing a nucleic acid molecule annealed with at least one primer elongated and fixed onto a surface so that the nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of a labeled nucleotide to a polymerase and nucleotides comprising a base and a label; and

(b) imaging the labeled nucleotide added onto the primers;

to determine the nucleotide sequence of the nucleic acid molecule by the addition of the labeled dideoxy nucleotide.

47. A method of determining the nucleotide sequence of an individual-nucleic acid molecule, comprising:

(a) exposing a nucleic acid molecule annealed with at least one primer elongated and fixed onto a surface so that the nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of labeled nucleotides to a polymerase and dideoxy nucleotides;

(b) exposing the nucleic acid molecule annealed with at least one primer to a polymerase and nucleotides including nucleotides comprising a label to produce a labeled primer extension nucleic acid molecule; and

(c) imaging the labeled primer extension nucleic acid molecule to produce an image;

to determine the nucleotide sequence of the nucleic acid molecule by the absence of a primer extension product corresponding to the dideoxy nucleotides used in step (a).

48. A method of determining the nucleotide sequence of an individual nucleic acid molecule, comprising:

(a) elongating and fixing the nucleic acid molecule onto a surface so that the nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of labeled nucleotides;

(b) annealing at least one primer to the elongated and fixed nucleic acid molecule;

(c) exposing the nucleic acid molecule annealed with a primer to a polymerase and dideoxy nucleotides;

(d) exposing the nucleic acid molecule to a polymerase and nucleotides including nucleotides comprising a label to produce at least one labeled primer extension nucleic acid molecule; and

(e) imaging the labeled primer extension nucleic acid molecule to produce an image;

to determine the nucleotide sequence of the nucleic acid molecule by the absence of a primer extension product corresponding to the dideoxy nucleotides used in step (c).

49. A system for determining the nucleotide sequence of an individual nucleic acid molecule, comprising:

(a) an elongated and fixed nucleic acid molecule on a surface so that the nucleic acid molecules remain accessible for enzymatic reactions with enzymes for the addition of labeled nucleotides;

(b) at least one primer annealed to the nucleic acid molecule;

(c) a polymerase enzyme fixed on the surface to produce a primer extension product;

(d) dideoxy nucleotides fixed on the surface;

(e) nucleotides comprising a label fixed on the surface; and

(f) a device for imaging the elongated and fixed nucleic acid molecule to detect the presence of labeled nucleotides in the primer extension product to produce an image;

whereby the absence of the image of the primer extension product for a particular dideoxy nucleotide corresponds to the nucleotide sequence at one position of the nucleic acid molecule.

50. A system for determining a single nucleotide polymorphism in a population of nucleic acid molecules, comprising the system of claim 47, in which the nucleic acid molecules are elongated and fixed onto at least four surfaces and the surfaces are individually exposed to dideoxynucleotides comprising different bases.

51. A method for imaging multiple labeled nucleotides on an individual double

stranded nucleic acid molecule, comprising:

(a) nicking a nucleic acid molecule elongated and fixed onto a surface so that the double stranded nucleic acid molecule remains accessible for enzymatic reactions with enzymes for the addition of labeled nucleotides;

(b) enzymatically adding multiple nucleotides comprising at least four bases and at least four labels; and (c) simultaneously imaging the added labels.

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PATENT APPLICATION FULL TEXT AND IMAGE DATABASE

United States Patent Application *20030096318*
Kind Code **A1**
Schubert, Walter **May 22, 2003**

Method for identifying cell specific proteins

Abstract

The present invention relates to a method for identifying cell-specific proteins comprising the following steps: a) determining cell-specific protein combination patterns of n cells; b) comparing the protein combination patterns of healthy and pathologically or physiologically modified cells of one cell type or comparing the protein combination patterns of cells of a different cell type affected by the same disease; c1) subtracting the coincident parts of the protein combination patterns of healthy and pathologically or physiologically modified cells of one cell type compared in step b) and determining a cell-specific protein resulting therefrom; or c2) subtracting the non-coincident parts of the protein combination patterns of cells of a different cell type affected by the same disease compared in step b) and determining a cell-specific protein resulting therefrom; and d) identifying the resulting cell-specific protein in terms of molecules and spatial structure.

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Foreign Application Data

Date	Code	Application Number
Sep 4, 2000	DE	100 43 470.3

Claims

1. A method for identifying cell-specific proteins comprising the following steps: a) determining cell-specific protein combination patterns of n cells; b) comparing the protein combination patterns of healthy and pathologically or physiologically modified cells of one cell type or comparing the protein combination patterns of cells of a different cell type affected by the same disease; c1) subtracting the coincident parts of the protein combination patterns of healthy and pathologically or physiologically modified cells of one cell type compared in step b) and determining a cell-specific protein resulting therefrom; or c2) subtracting the non-coincident parts of the protein combination patterns of cells of a different cell type affected by the same disease compared in step b) and determining a cell-specific protein resulting therefrom; and d) identifying the resulting cell-specific protein in terms of molecules and spatial structure.

2. The method as claimed in claim 1 characterized in that said method comprises the selection of a substance for suppressing the activity of the identified cell-specific protein.

3. The method as claimed in claim 2 characterized in that said substance is an antibody.

4. The method as claimed in one of the preceding claims characterized in that pathologically modified cells are of the invasive type.

Description

DESCRIPTION

[0001] The present invention relates to a method for identifying cell-specific proteins.

[0002] The identification of cell-specific protein combination patterns is a crucial factor for elucidating cell-to-cell interactions which may cause countless effects within an organism. Especially the knowledge of disease-specific target structures is a decisive prerequisite for the development of effective medications which at the same time have only few side-effects.

[0003] It is known that immune cells (lymphocytes) will express specific protein combinations--also referred to as protein combination patterns or (abbreviated) PCP--which are responsible for a binding to endothelial cells of the blood vessels in the brain and in muscle tissue. Other protein combinations, by contrast, will not cause such binding to these endothelial cells. Surprisingly, these specific combinations are inter-individually constant, always exhibiting the same binding functions. The specific protein combination patterns therefore seem to be an inter-individually constant lymphocyte binding code of the cell surface for organ-specific endothelial cell surfaces which constitutes a cell-specific target structure.

Cell-specific target structures may thus include very specific protein combination patterns.

[0004] Invasive tumor cells also exhibit specific protein combination patterns on their cell surfaces which result in a specific, i.e. organ-selective, invasive behavior. Such protein combination patterns therefore constitute target structures for potential medications.

[0005] However, an absolute prerequisite for the development of such highly selective medications is the knowledge of the molecular composition of these target structures.

[0006] Methods for identifying target structures are known in the prior art, which are based on the analysis of gene expression profiles of diseased tissues or cells as compared to gene expression profiles of healthy tissues or cells, with protein expression profiles as well as expression profiles of the messenger ribonucleic acid (mRNA) being intended to provide information on the appearance of new proteins, malregulated or abnormally modified proteins in diseased tissues or cells (e.g. in: F. Lottspeich/H. Zorbas; Bioanalytik; Spektrum Akademischer Verlag; Heidelberg, 1998).

[0007] However, these methods all use cell homogenates usually produced from thousands or millions of cells since only such vast amounts of cells will allow expression profiles of the abovementioned kind to be established. The cells contained in the cell homogenates have been solubilized so as to allow the extraction and separation of the proteins or mRNA molecules by means of biochemical processes.

[0008] A shortcoming of these prior art methods, however, is that they are not suitable for identifying protein combination patterns, since the individual protein components of such a protein combination pattern will be completely separated by the generation of cell homogenates and by the subsequent extraction processes, and the fundamental information relating to their cell- and tissue-topological location will be lost. Furthermore, owing to the destruction of the cell compartments, no information can be gained any longer regarding the combinations of proteins within these cell compartments and their relative topological relation to each other.

[0009] Moreover, another disadvantage of the prior art processes is that no analyses can be performed at an individual level, making it impossible to detect differences of the individual cells with respect to their protein combination patterns. These disadvantages are overcome by the methods disclosed in DE 197 09 348 C2 and DE 100 01 685 A1 for determining, identifying and mapping cell-specific target structures. These methods can be used for comparatively examining protein combination patterns of individual cells or cell membranes of different cell or tissue samples. In doing so, those marker molecules can be identified which will bind to e.g. a certain protein combination pattern or to a certain area of such a protein combination pattern of a first object stemming from a first tissue or cell sample, and which will at the same time not bind to a second object stemming from a second tissue or cell sample. By means of these identified marker molecules, using a sample portion of the first tissue and/or cell sample, those molecular areas (molecules or molecular complexes) of the protein combination pattern may now be located and/or selected and subsequently characterized which are bound by the identified marker molecules. This will allow the detection and understanding of the molecular composition of a protein combination pattern, of the arrangement of the molecules within said protein combination pattern as well as of the arrangement of the protein combination pattern within a tissue or a cell.

[0010] The cell-specific protein combination patterns thus obtained, however, will still be highly complex--which will clearly aggravate the development of highly selective medications.

[0011] It is therefore the object of the present invention to further improve on and provide a method of the above-mentioned type which will further process identified and highly complex protein combination patterns, thus facilitating the development of highly selective medications.

[0012] This object is accomplished by a method of the invention for identifying cell-specific proteins comprising the following steps: (a) determining cell-specific protein combination patterns of n cells; (b) comparing the protein combination patterns of healthy and pathologically or physiologically modified cells of one cell type or comparing the protein combination patterns of cells of a different cell type affected by the same disease; (c1) subtracting the coincident parts of the protein combination patterns of healthy and pathologically or physiologically modified cells of one cell type compared in step (b) and determining a cell-specific protein resulting therefrom; or (c2) subtracting the non-coincident parts of the protein combination patterns of cells of a different cell type affected by the same disease compared in step (b) and determining a cell-specific protein resulting therefrom; and (d) identifying the resulting cell-specific protein in terms of molecules and spatial structure.

[0013] Reducing the highly complex protein combination patterns thus determined to a single, highly selective and cell-specific protein will clearly facilitate the development of likewise highly selective medications, at the same time significantly shortening the time required for such development. Thus it will no longer be required in the development of medications to investigate the highly complex and likewise cell-characteristic protein combination patterns.

[0014] The invention merely requires a selection of a substance for suppressing the activity of the identified cell-specific protein. Such suppression will cause the cell-specific protein network, and hence the cell functions, to collapse. For example, switching off the cell-specific protein of tumor cells will in turn suppress the migration of these cells since the protein identified in this process controls and regulates the migration behavior of the tumor cell. The suppressing substance in this case may be an antibody.

[0015] Particular advantages of the method according to the invention will be obtained if pathologically modified cells are of the invasive type.

[0016] The knowledge of these e.g. disease-specific proteins within a protein combination pattern will moreover allow the development of highly specific medications which will be almost without undesired side effects owing to this very specificity.

[0017] The cell-specific protein combination patterns to be processed according to the invention will be determined by means of the methods disclosed in DE 197 09 348 C2 and DE 100 01 685 A1 for determining, identifying and mapping cell-specific target structures.

* * * * *